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DEVOTED TO GASTRO-ENTEROLOGY AND NUTRITION

ORIGINAL CONTRIBUTIONS

Volume 22 July, 1955 Number 7

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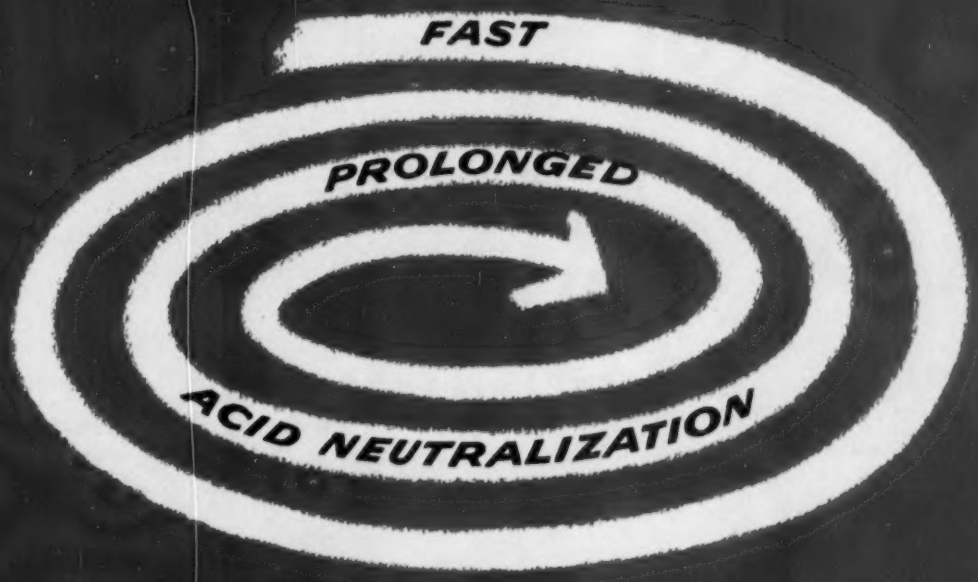

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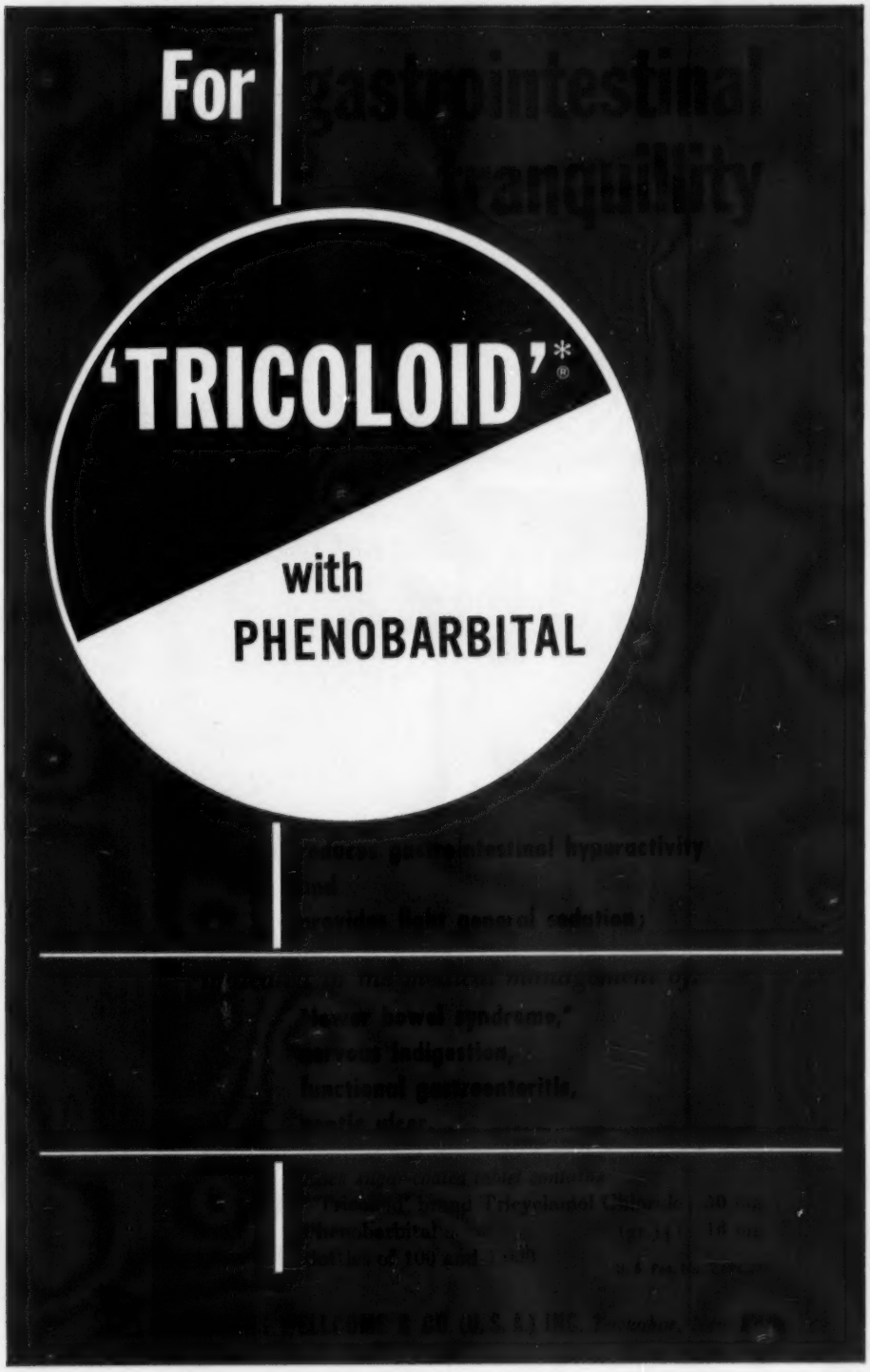
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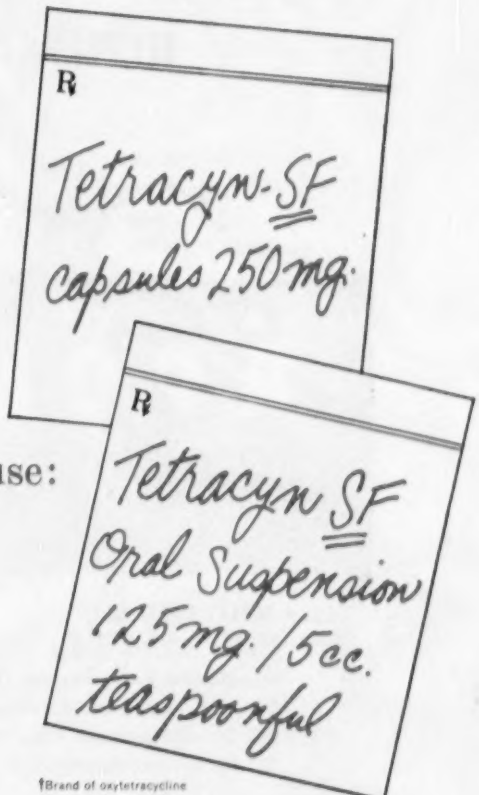

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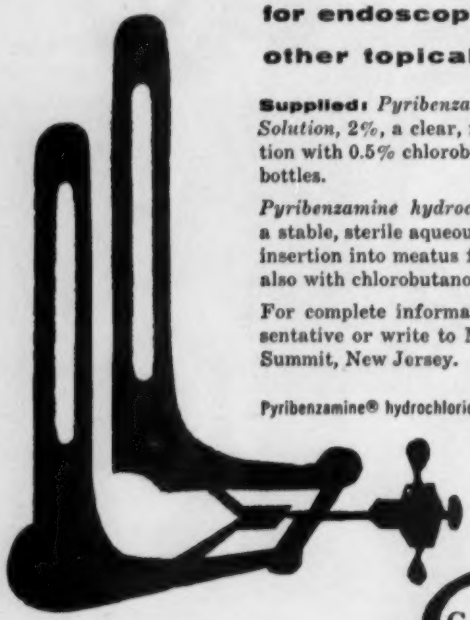

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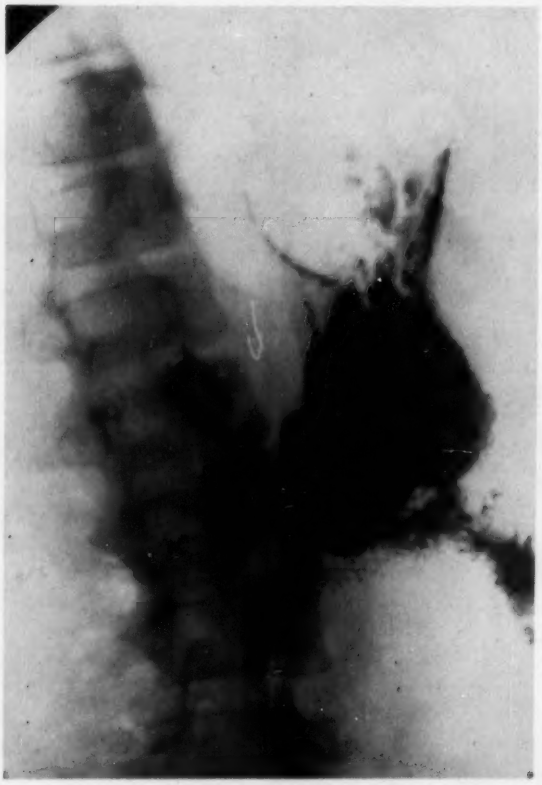
ROENTGENOLOGICAL FINDINGS IN GASTRIC AND DUODENAL ULCERS IN CHILDREN

FRANZ J. LUST, M.D., F.A.C.G., New York, N. Y.*

IN 1953 AYE reported four cases of peptic ulcers of the stomach in children. In the past twenty years only 20 cases of gastric ulcers have been reported in the literature, which Aye has surveyed. It is astonishing that only such a small number of cases has been discovered. Brenner, in 500 routine autopsies in children, reported an incidence of duodenal ulcers of 1.4%. Bird and his colleagues, in a careful review of the entire literature, discovered only 243 cases of peptic ulcer, approximately half of which were found at autopsies and the remaining half at operation. From the histories of these cases, Bird found evidence that many cases of peptic ulcer are not recognized in routine clinical practice. The incidence of these lesions is much higher than is generally believed.

Alexander published thirty cases of duodenal ulcers, the largest group ever reported. These lesions were discovered in the roentgenological examination of 250 children, who presented symptoms of gastrointestinal distress. In several instances in this series the patients had been studied for considerable lengths of time by various clinical methods before the true nature of their disease was recognized. Morgan has reviewed this topic and critically anaylzed the reports. Bird has pointed out that 70% of the patients reported with peptic ulcer between the ages of 7 and 15 years were operated upon. Most of the cases of gastric ulcers published before 1938, were treated surgically and found only during operation. Most of the textbooks on roentgenological diagnosis of the gastro-intestinal tract do not contain reproductions of gastric ulcers found in childhood. Buckstein in an elaborate book is able to show only one case of duodenal ulcer!



F.g. 1. Ulcer of the lesser curvature of a boy of 9 years. Note the large ulcer on the lesser curvature.

(From the Department of Radiology, Bellevue Hospital Center, Director Dr. Maxwell H. Poppel, New York City).
*Assistant Roentgenologist, Bellevue Hospital Center, New York City.

What is the reason for the discrepancy between ulcers in adults and ulcers in children? Why are so few cases of this disease in children found and reported? We do not have to discuss the high incidence of this disease in adults. Is it not astonishing that the surgical diagnosis of ulcers in adults is only a very rare one, whereas the roentgenological diagnosis is easy. In opposition to this well known fact we find that many more ulcers in children have to be treated surgically.

It has been our experience, that the routine roentgenological examination of the gastro-intestinal tract of children has been unsatisfactory. Even in big institutions, only very few cases have been referred to the radiological department for studies. Apparently, the pediatrician has not been very satisfied with the prevalent roentgenological studies. Another point is, apparently, the prevalent idea that ulcerating lesions of the upper gastro-intestinal tract are rarities. Very frequently, only after bleeding has taken place, have roentgenological studies been advised. We like to point out to pediatricians, who might not be aware of the fact, that even known ulcers in adults, in the first four weeks after bleeding, are extremely difficult to demonstrate. This clinical-roentgenological experience should be taken into consideration. The high incidence of necessary surgery may be due to the difficulty of diagnosis, which is only realized when medical treatment, which is so effective in adults, is too late.

We have tried to overcome the difficulties in children by evolving a new method in roentgenology, which is entirely different from that which has been recommended by Templeton and later by Morgan. In a previous publication, we have discussed the prevalence of roentgenography over fluoroscopy, reducing the latter method to a secondary position. Besides we have advocated the use of a shielded screen (Belloscope) for use in normal light. This feature of the examination, and the emphasis on removing any mental stress of the children, and of the parents as well, has, apparently, permitted us to achieve greater accuracy in our diagnostic procedure. Morgan has emphasized the use of repeated spotfilms. We heartily agree with his recom-

Fig. 2. Ulcer of the lesser curvature of a boy of 9 years. (See fig. 1). Note the large amount of gastric secretion 20 min. after administration of barium.

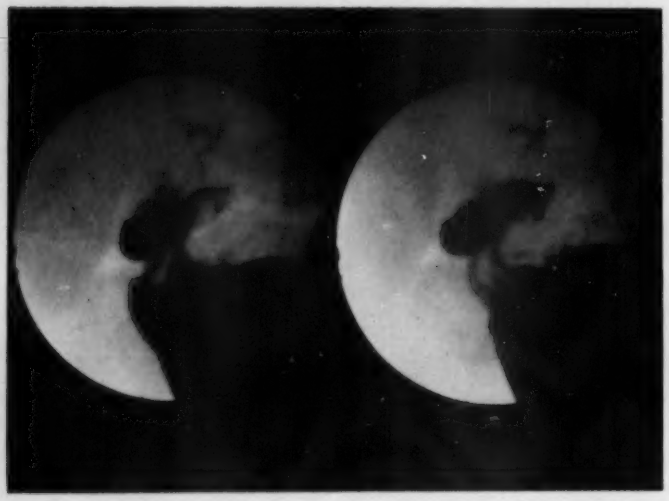


Fig. 3. Duodenal ulcer in a boy of five years. Note the sharp, deformity of the cap.

Fig. 4. Duodenal ulcer in a child of 12 years. The ulcer is seen on compression in the middle of the cap.

mendation. The difficulty encountered in children is, that up to now, this procedure had to be performed in the darkened fluoroscopic room, which is a great handicap as children are usually extremely frightened by dark rooms. The second difficulty is due to the extremely rapid transit of the contrast substance through the duodenum in children. The physician must have very great experience in order to make the exposures in rapid succession. In children, the lesions are so shallow that they can only be recognized after studying many exposures. In a previous communication of the study of gastric secretion, we have been able to point out changes which enable us to suspect pathology which might otherwise have escaped us.

Fig. 5. Same case as fig. 4. Six hours after administration of barium. Note the large gastric residue, giving pains hours after eating.

It is astonishing, without giving statistics of our work, how high the incidence of pathology seems to be, when these thorough methods are used. Within a short time we were able to detect a large ulcer of the lesser curvature of the stomach, otherwise considered to be a rarity.

The roentgenological signs of ulcers in children are the same as those seen in acute ulcers in adults. In these little patients, fibrosis has not set in, therefore the clinical experience of frequent perforations. The gastric ulcer shows a niche, as seen by all other authors. Niches on the greater curvature have not been described as yet. Most of the ulcers are on the distal half of the lesser curvature or in the region of the gastric antrum.

The diagnosis of an ulcer of the duodenum relies, too, on the demonstration of a niche. However, in several cases, the niche seems to be in the second portion of the duodenum. In some of our cases a very deformed duodenal bulb was visible.

We like to stress that, besides the organic signs, the functional pathology in these cases is of importance. The studies of the gastric secretion, as reported in a previous publication, are important, for they reveal, without the use of the stomach tube, that a gastric hypersecretion is present. The second functional pathology is that of delayed, gastric emptying. We emphasize the studies six hours after ingestion of the contrast suspension. If, as seen on fig. 5 a large gastric retention is demonstrable, it is not astonishing that our little patients complain of discomfort hours after meals. This

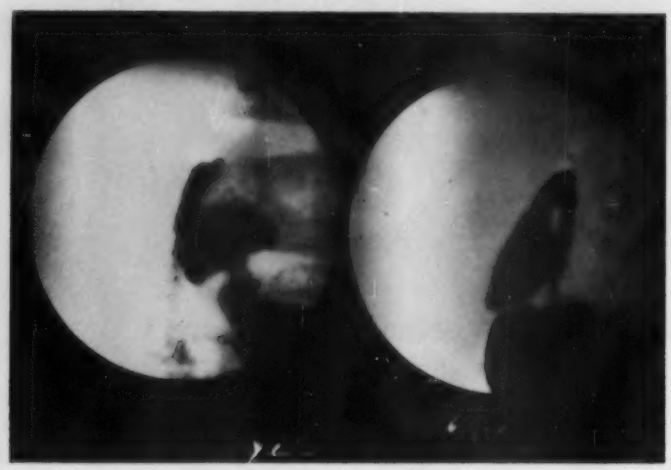


Fig. 6. Duodenal ulcer in a child 9 years old. Only repeated spotfilms demonstrate a lesion, not visible during fluoroscopy.

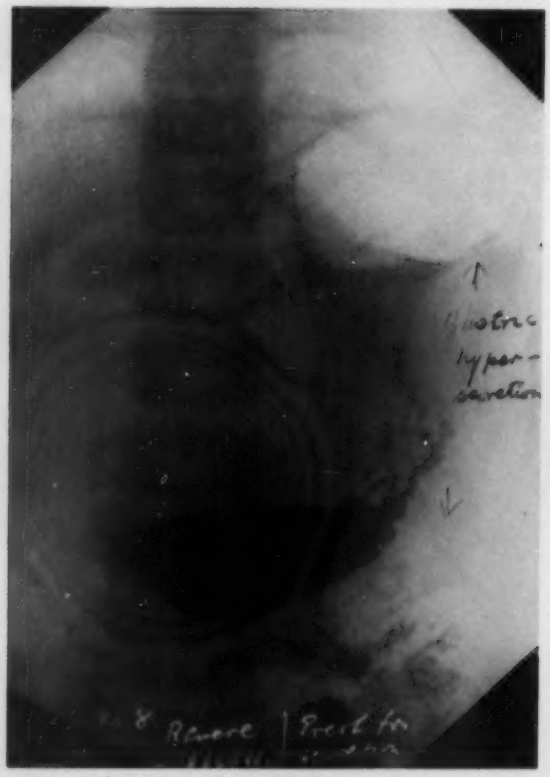


Fig. 7. Same case as fig. 6. Note the large amount of gastric secretion 20 minutes after administration of barium.

is not due to an organic stenosis, which is ruled out by the studies of stomach and duodenum.

SUMMARY

The roentgenological examination of children with abdominal symptoms is of the greatest importance, as, apparently, the diagnosis of peptic ulcers in childhood is frequently missed. Only by using all modern methods of roentgenology is an improvement in the diagnosis possible. Due to the small size of the pathological process, fluoroscopy is unable to detect the lesion. Besides, the motility of the alimentary tract is so rapid that the fluoroscopist cannot detect the lesions. Therefore, multiple roentgenograms are necessary and still more spotfilms of the very rapid moving parts of the duodenum are indicated. It is astonishing at what an early age deformities due to ulcers can be found. Some of the complaints of the patients are due, not only to the actual ulcer, but also to the concomitant functional pathology, such as hypersecretion and delayed emptying of the stomach. The study of gastric hypersecretion and increased mucous production has been dealt with before; however, it is nearly always present in ulcer cases. The delayed motility (six hour gastric residue) plays an important role as a cause for some of the complaints.

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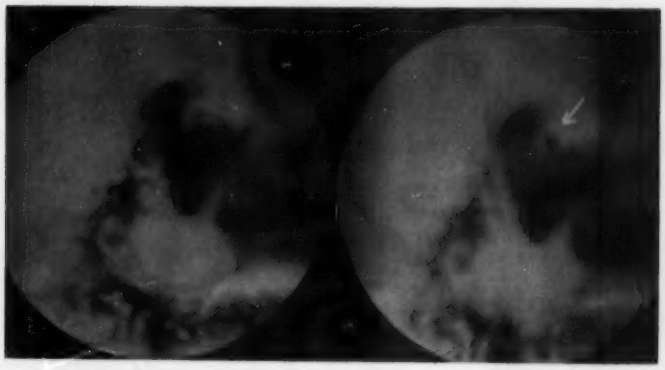

Fig. 8. Duodenal ulcer in boy of 5 years. The ulcer was best seen on repeated spotfilms. The fluoroscopy was inconclusive.

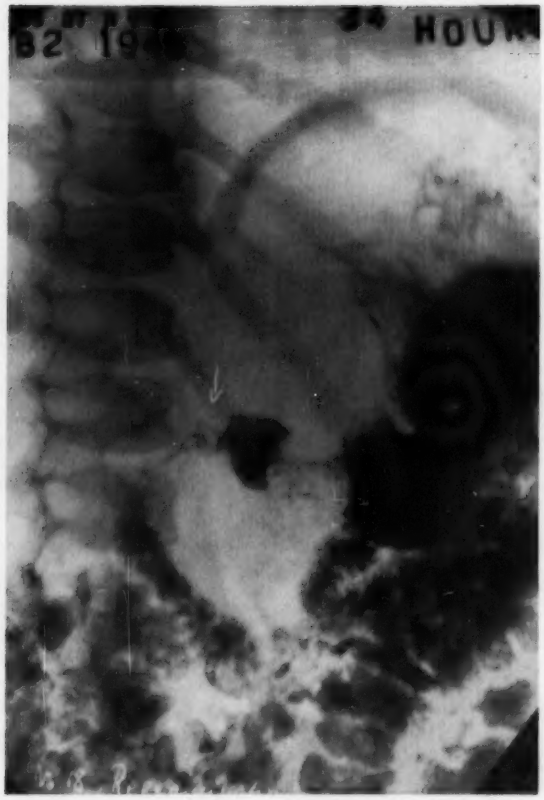

Fig. 9. Duodenal ulcer in a boy of 6 years. The niche in the duodenal cap was a constant finding.

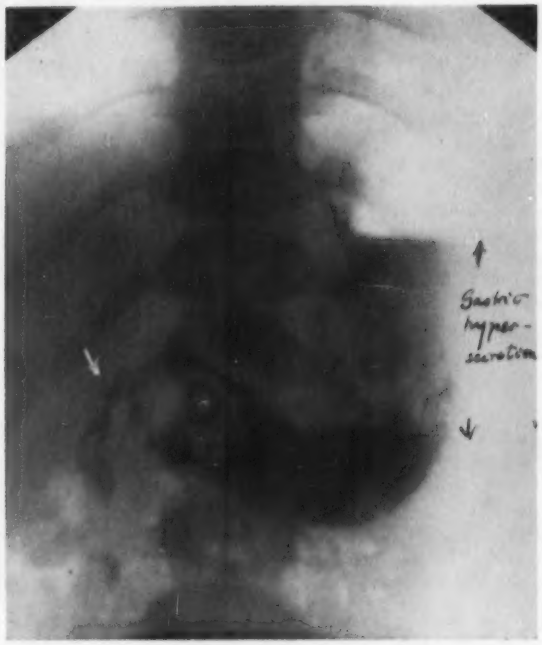

Fig. 10. Same case as fig. 9. Films taken 2 years later. Duodenal ulcer.

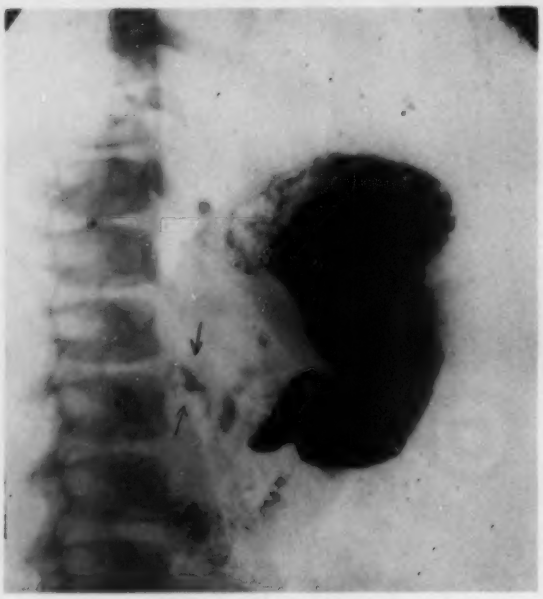

Fig. 11. Same case as fig. 9 and 10. Duodenal ulcer. The patient was now 10 years old and had suffered a haemorrhage, which necessitated hospitalization. This examination was performed two years after fig. 10.

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CLINICAL EXPERIENCES WITH THE SPLENIC FLEXURE SYNDROME AND THE HEPATIC FLEXURE SYNDROME

EDDY D. PALMER, LT. COL., M.C.*, DAVID L. DEUTSCH, LT. COL., M.C.*, AND NORMAN M. SCOTT, JR., MAJ., M.C.*, Washington, D. C.

AMONG RECENTLY expounded clinical concepts, that of the hepatic and splenic flexure syndromes has been of the greatest practical help in our ambulatory gastroenterologic practice. This very simple concept, which we had no doubt previously looked at without seeing in hundreds of patients, has permitted definitive thinking in many instances of upper abdominal distress which otherwise would have constituted difficult clinical problems. The purpose of this communication is to direct more attention to the hepatic and splenic flexure syndromes because to us they are much more important than their scant publicity might suggest.

It is difficult to become excited over gas in the colon as a cause of symptoms. Everyone has gas—it is normal—and, unless there be actual colon disease, it can do no physical harm there. Similarly, most people feel rather confident that they know and can recognize the sensations produced by gas in the colon, and it is easy for the doctor to agree. Nevertheless, for many years the role of excess colon gas in the occasional production of a variety of obscure upper abdominal and chest symptoms has been well recognized. It remained for Machella, Dworken and Biel (2) to draw the matter of symptomatic colon gas into focus. In a particularly significant study, they proposed the clinical importance of the "splenic flexure syndrome," as illustrated in 40 patients, and showed that the syndrome could be reproduced in these patients and in most control subjects by artificial distention of the splenic flexure by balloon insufflation (1).

Since the presentation of the observations of Machella and colleagues at the 53rd Annual Meeting of the American Gastroenterological Association, May 1952 (1), we have treated 85 patients with the diagnosis of splenic flexure syndrome, hepatic flexure syndrome, or both. Although the first was commonest, the right-sided variety of the syndrome has proved to be of equal clinical significance and cannot be excluded from any discussion of the splenic flexure syndrome. This paper recounts our clinical experiences with and impressions gained from these 85 patients.

This material has been reviewed and there is no objection to publication by the Office of the Surgeon General, Department of the Army. Medc. Oct. 26, 1954.

*Gastroenterology Service, Walter Reed Army Hospital, Washington, D. C.

Submitted Jan. 24, 1955.

PATIENT GROUP

In the present series there were more men than women, but the composition of the clinic population is predominantly male. It is our impression that there

is no important sex predilection. Less than 10% of the patients were Negroes. The ages at the time of diagnosis were distributed rather evenly between 31 and 70 years. Half of the patients had had symptoms less than two years at the time of diagnosis, and half more than two and up to 40 years.

Almost all of the patients had been studied rather thoroughly on a few or several occasions in the past. Most often, the symptomatic picture had caused investigation to be directed especially at either the heart or the gall bladder. A heavy envelope of x-ray films accompanied most patients.

EMOTIONAL CHARACTERISTICS OF THE PATIENTS

Although Machella and colleagues have emphasized the "trap-like" mechanism produced by the splenic flexure in the steeple type of colon, we have been as much impressed by the functional as by the purely mechanical set-up in these patients. Although it is no argument, it is noteworthy that the configurations assumed by this most plastic organ are not closely correlated with the presence or absence of the splenic and hepatic flexure syndromes.

Although we at first considered these syndromes as irritable-bowel equivalents, as experience accumulated it became evident that often a different type of personality is implicated. The patient is not as overtly nervous. There is often the confidence, hostility and general tension of the ulcer patient. Separations are not emotionally traumatic, and the search for security does not include establishment of deep-rooted attachments. The patients may be drifters, easily dissatisfied, skeptical, calculating, argumentative. They don't follow prescribed treatment gracefully and often exert their hostilities by open criticism of professional personnel. Above all, there seems to be a conscious effort to miss the point in all their communications. Characteristically there is little bowel consciousness, and, in fact, the patient is often dissatisfied with the explanation that the colon is responsible for the symptoms. This attitude may well have had its nidus in the unsuccessful diagnostic probing by many physicians, none ever able to give a certain answer to the problem or satisfactory treatment.

SYMPTOMS

Symptomatically, splenic flexure syndrome and hepatic flexure syndrome differ considerably. The former is characterized particularly by low left anterior chest discomfort, at times with radiation to the epigastrium, the left flank or left renal areas. The discomfort may, in fact, be limited to these latter areas. The sensation is one of moderately severe distention or pressure discomfort, poorly localized, often stimulating a fruitless effort to belch, at times a little frightening to the patient, at times aggravated by full inspiration. The symptoms appear in attacks, usually with a brisk onset, and last from several minutes to a few hours. There is rarely a cramping element. Recumbency doesn't appear to have an important influence over the symptoms. Postprandial periods tend to be most uncomfortable for the patient. Palpitation, periodic breathlessness, and anorexia are occasional complaints. Excess flatus is not a consistent symptom, but at times a bowel movement or passage of flatus is associated with relief. Rarely are there bowel complaints per se, constipation being encountered most frequently. The patient usually interprets his symptoms as indicative of heart or left lung disease, and the clinician often finds it necessary to give some thought to these two organs.

Fig. 1. X-ray film made during barium contrast study showing gas trapped in splenic and hepatic flexures.

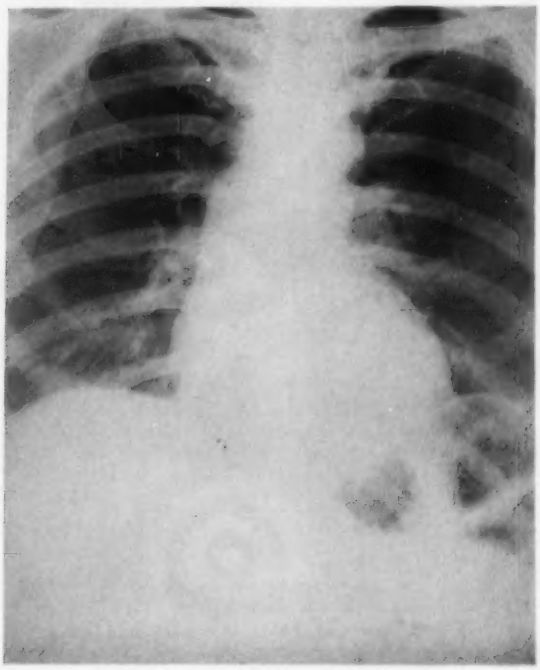

Fig. 2. Routine P-A chest film. The gas trapped in the splenic flexure elevates the diaphragm.

Subjectively, the hepatic flexure syndrome simulates gall bladder disease. The main symptom is that of periodic right upper quadrant pressure discomfort, at times severe. It may occasionally be crampy and rarely has a burning quality. Over the weeks and months it shows wide and erratic variations in severity. The discomfort is usually localized rather closely to the gall bladder region. At times it seems to travel between the gall bladder area and epigastrium or left upper quadrant. There occasionally is pain in the right kidney area of the back and in the right shoulder. Usually there is, in addition, a variety of simple dyspeptic symptoms. Thus, the symptoms are usually most annoying after meals. The patient feels best when his stomach is empty. Fullness, nonproductive desire to belch, aggravation by "gaseous" foods, other food idiosyncrasies, easy nausea, and borborygmi, are rather common.

SIGNS

Only one patient, who had had the splenic flexure syndrome for two years, had striking physical findings. She was found to have prominent flaring of the left subcostal edge anteriorly and laterally during spells of discomfort. There was little distention of the abdominal wall at such times.

In all patients with splenic flexure syndrome the gas accumulations can easily be detected by percussion. A clear, tympanitic note is elicited as high as the fifth intercostal space in the mid-axillary line.

ROENTGENOLOGIC FINDINGS

This is a clinical diagnosis, to be supported by certain radiologic findings. The demonstration of large amounts of gas persisting in the hepatic or splenic flexure does not by itself permit a diagnosis, and cannot be considered an abnormal finding unless it is correlated clinically with certain symptoms.

During symptomatic periods, x-ray films which include the upper abdomen regularly reveal collections of gas rather sharply localized to one or both flexures (fig. 1). On numerous occasions a simple routine chest film has incidentally shown a high, distended splenic flexure (fig. 2). The gas remains stationary throughout the symptomatic period. Rarely is there excess gas elsewhere in the bowel, although at times the Magenblase may be rather large. Characteristically, the splenic flexure lies high in the abdomen and its gas bubble often appears to contact the diaphragmatic profile (fig. 2 & 3). When it is the hepatic flexure which is involved, cholecystogram may show the gas bubble in intimate relationship to the gall bladder (fig. 4).

DIFFERENTIAL DIAGNOSIS

All of our patients had been referred from other clinics or medical facilities. The referral impressions and diagnoses furnished interesting information regarding differential diagnosis. The basic neurosis involved in the illness had been noted in most instances, but there had been something about the patients which had made successive examiners uneasy over the possibility of underlying organic disease. In cases of hepatic flexure syndrome this was invariably obscure chronic liver disease or chronic biliary tract disease. Noncalculous chronic cholecystitis, biliary dyskinesia, and postcholecystectomy syndrome were the common diagnoses suggested in referral. Several of the patients had had a cholecystectomy in the past, without relief, and now were thought probably to have a form of postcholecystectomy disease.

The common diagnostic possibilities mentioned in cases of splenic flexure syndrome were various types

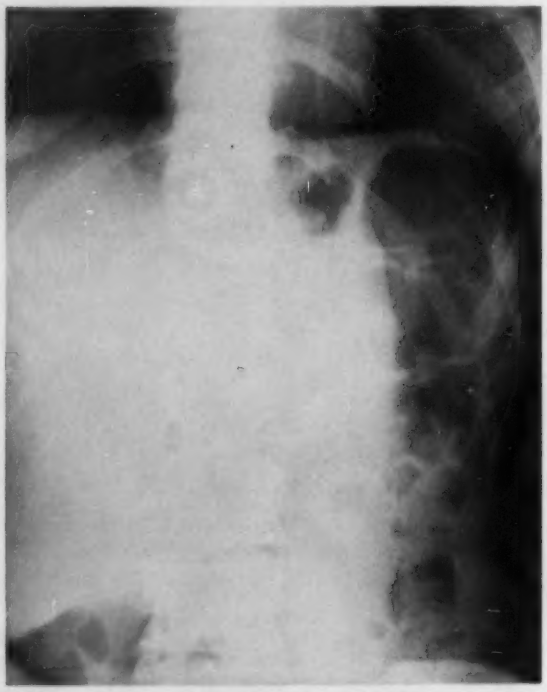

Fig. 3. The gas trapped in the descending colon and splenic flexure was demonstrated in every film taken of this patient's abdomen during symptomatic periods. Coronary artery insufficiency had been suspected but could not be confirmed.

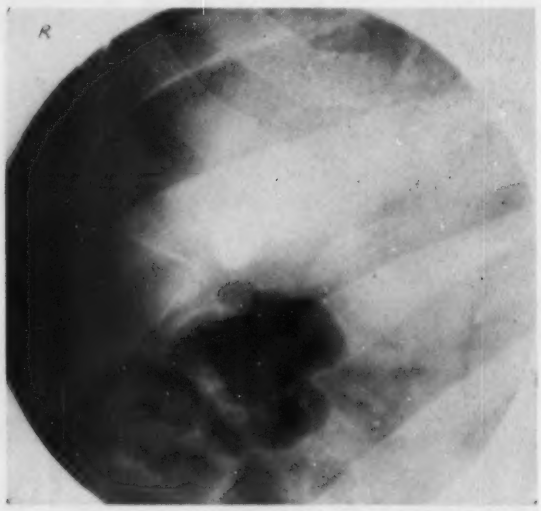

Fig. 4. Cholecystogram made during a symptomatic period in this patient whose complaints suggested gall bladder disease. The gall bladder filled and functioned normally. The persistence of the gas bubble near the gall bladder appeared to explain the symptoms.

of heart disease, hiatus hernia, and gastric ulcer. Less commonly gastric cancer, pancreatic tumor, and left kidney disease had been mentioned.

TREATMENT

Treatment has been difficult to implement in the majority of cases. It has been our conviction that in this situation it is the clinician's responsibility to go directly to the psychotherapeutic approach. This is difficult because this is an especially non-receptive group of patients. Part of our trouble has, no doubt, been our unskilled approach to psychotherapy, but we firmly believe that the patient's doctor—his internist—should carry out the therapy. Our experience has suggested that a minimum of between five and 10 hours of interviewing are required for any degree of help.

In many instances it has been necessary to forego active psychotherapy because the situation did not permit free access to the patient. We soon found that none of the common colon medications were especially useful—the sedatives, adsorptives, antispasmodics, bulk-producers, etc., have all been tried. Dr. Lee Miller, of the U. S. Soldier's Home Hospital, Washington, D. C., urged us to try asafoetida. This we did, with tongue in cheek, but have found asafoetida to be far the most helpful medication. When taken in a dose of 0.3 gm. with each meal, approximately half of the patients have experienced good symptomatic relief. Except for its mild antispasmodic activity, we know of no reason why asafoetida should help. Drugs which are physiologically more active lack its attributes when used in treatment of the flexure syndromes.

COMMENT

The splenic flexure and hepatic flexure syndromes have filled a distinct gap in the differential diagnostic spectrum for patients whose symptoms suggest cardiac, renal, or more serious upper gastrointestinal disease. It enables the physician confidently to reassure himself and the patient that the symptoms do not mean heart disease nor necessitate an operation. This reassurance may, in itself, help to offset the doctor's inability to offer any spectacular treatment of the patient's symptoms.

Since most of our cases were referred after multiple tests had failed to show positive evidence of organic disease ordinarily suggested by the symptoms, it might appear that the diagnosis of the flexure syndromes is one of exclusion. Such is not the case; there is little doubt in our minds as to their validity as clinical entities, readily lending themselves to positive diagnosis. It is clear, however, that the presence of gas in the flexures is not necessarily productive of symptoms. A small but significant group of such patients has been observed in whom cholelithiasis, nephrolithiasis and coronary artery insufficiency actually proved to exist. A positive diagnostic attitude toward the flexure syndromes is not compromised by employment of routine clinical and laboratory procedures to exclude the more serious conditions suggested by the patient's symptoms.

In a busy clinic, such a new diagnostic "gimmick" often tends to be utilized with a degree of enthusiasm which in retrospect cannot be justified. This we have earnestly tried to avoid. A broad range of usefulness was still obtained. Once we became aware of the flexure syndromes as helpful clinical entities, the accumulation of the 85 cases reported here took a surprisingly short time. We have tried in this report to republicize the concept of the flexure syndromes as clinically useful, by presenting a general summary of our experiences with them.

CONCLUSION

Excess gas in the hepatic flexure or splenic flexure of the colon, although in itself not unusual nor necessarily significant, may at times be the explanation for symptoms suggesting cardiac, stomach, gall bladder, kidney or pulmonary disease. The concept of the hepatic and splenic flexure syndromes has proved to be of positive clinical value.

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HUNGER

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THE PROBLEM of hunger deserves the attention of the medical world as it has so many factors involved in it and therefore deserves close attention and understanding. There are many factors in the cure and treatment of diabetics alone that may contribute to a better understanding of hunger and as my own experience has been primarily the treatment of diabetics, I shall confine my observations largely to the diabetic problem.

It often happens that when diabetes is discovered, the physician introduces a factor of fear into the mind of the patient. In order to make the patient follow instructions, he tells too much; he speaks of all the possible complications in diabetes, the gangrene requiring amputation of a leg, the coma which may cause death, the "insulin shock" (incidentally this is a bad psychological term for "insulin reaction") which simply scares the patient out of his wits, of arteriosclerosis in diabetics, retinitis often leading to blindness, of the kidney involvements from which one can die etc., etc.

It is no wonder that patients are afraid to use insulin when they hear about "insulin shocks" which to them means "next door to death." Invariably a patient will say: "Doctor I would do anything just so I will not have to use insulin!" The fault is not with the patient but with the doctor who has not used good judgment. The fault lies largely in the present teaching in the medical schools where the psychological aspect

of medicine receives little or no consideration. There is where it should be corrected, for the student needs to know not only the scientific aspect of medicine but the psychological aspect of it as well. It is well to know "what to do" but it is equally important to know "what not to do."

MAN MADE HUNGER

Here I wish to consider the condition which is so predominant in the routine treatment of diabetes. The patient is directed to take, let us say 20 units of PZI and 10 units of Insulin in the morning. Then he is advised to examine his urine and if sugar is found at noon to take 6 to 8 additional units of Insulin at noon. And to follow the same procedure in the evening.

Here it is taken for granted that glycosuria is an index to the blood sugar level, namely that when glycosuria is found, one must assume that the blood sugar is high. This has been the general teaching in the medical schools, the hospitals and the clinics.

Were it only so, for thus our problem and the patient's would be greatly simplified. But, glycosuria is not a reliable index to glycemia, as I have repeatedly shown in previous writings (1). From these publications I will cite but one case which illustrates the problem. A little girl, 6 years of age, taking 15 units PZI and 15 units of Insulin in the morning. Her blood sugars at 8, 11, 4 were 108, 78, 40 mg. per cent and there was a heavy glycosuria in all three specimens, heaviest at noon. Had this child's diabetic condition been managed on the strength of the glycosuria findings alone, she would have been given at noon, when the glycosuria was heavy, some 6 to 10 additional units of Insulin. You can readily see what would have happened. Since the blood sugar at noon was 78 mg. per cent, more insulin given at this time certainly would have produced an insulin reaction, for even without ANY "extra" insulin, the evening blood sugar was 40 mg. per cent. This shows the folly of trying to substitute urine examinations (which so often are misleading) for blood sugar examinations which prove the actual facts in the matter.

In the above case there is also the other side of the problem. In the evening there is considerable hypoglycemia and when there is a hypoglycemia the patient is hungry; a man-made hunger. Since the fasting blood sugar is normal the PZI dosage in this case is correct and certainly cannot be increased, for an increase in the PZI would produce reaction the next morning. Here we need to make a slight reduction in the "insulin" in order to eliminate the evening hypoglycemia and then recheck and see what we have accomplished.

Now what happens when we induce hypoglycemia and the accompanying hunger with it? It is obvious that a person who is very hungry, be he a child or an adult, will eat. If you deny him food he will steal food, for he is in such a state that food is the only and all-important physiological necessity and the only thing which will correct his hunger. You can see how such a patient is DRIVEN into breaking his diet, not because he wants to, but because of unwise management. When patients eat under these conditions, it is a simple question of self-preservation: a response to a unique and primitive impulse.

HUNGER DUE TO UNCONTROLLED DIABETES

Before a patient is diagnosed as a diabetic, when he has been carrying high hyperglycemia unknown to himself and, as a result of it, losing much sugar through the urine (80 to 160 gm. in 24 hrs.), such a patient is always hungry for the simple reason that he has not been utilizing the excessive amount of food taken. Should he go on in this way, then eventually he begins to lose weight, not because he was not taking in an adequate number of calories, but because his body was not utilizing these calories due to an inadequate supply of insulin in the body. Here is hunger due to the inability of the patient to utilize his food.

Such a thing can happen even to a person taking insulin. If he needs, let us say 80 units a day, and he is taking only 20 units a day, he is apt to be running hyperglycemia most of the time and thus excreting a great deal of sugar. Thus, a restricted diet, minus what he loses through the urine, is simply inadequate and he will be hungry. It is a point to bear in mind.

HUNGER FROM OVEREXERCISE

A patient may be well adjusted on his diet and his insulin while in the hospital. In the hospital he was inactive, and it took, let us say 40 units of insulin a day for his control. Then he leaves the hospital. The type of work he goes back to requires a great deal of physical exercise, or in case of children, they become very active at play and sports. The result is repeated insulin reactions, for the dosage of insulin which was correct when the patient was in an inactive state, now becomes an overdosage. "Reactions," which mean hypoglycemia, result, and this brings on hunger. And a hungry person WILL eat, for it is the only thing which gives him relief. One must bear this in mind and try to compensate for the extra exercise with a correct insulin dosage as well as diet.

PSYCHOLOGICAL HUNGER

This we see frequently in diabetes, especially in those who have been accustomed to eating liberally. Restriction in diet in these patients makes them crave the very things which have been eliminated. This is only natural. We see it all around us in non-diabetics as well as diabetics. A wise physician will bear this in mind and handle such a patient in such manner as to minimize this psychological factor. In place of telling the patient of all the things he cannot have, he will approach the problem and tell him of all the things he CAN have. While we call this psychology, it is just common ordinary sense. It is NOT what diabetics eat, but HOW MUCH they eat, which is the kernel of the problem. The thing to eliminate here is any abnormal psychological attitude toward food. Eating is a habit. One can develop a habit of eating moderately, or of eating excessively. The thing to point out to the patient is, that excessive eating, whether in a diabetic or a non-diabetic, is bad and carries with it too severe a penalty in the end. If a doctor puts the problem on such a basis, he will convince the patient.

HUNGER IN HYPERINSULINISM

The hunger we meet with in hyperinsulinism, or chronic hypoglycemia, is due to hypoglycemia. Whenever hypoglycemia is present, we deal with hunger.

What usually happens is that such a patient has been given a high carbohydrate diet, plus feeding between meal and at bed time, with carbohydrate, in an attempt to prevent the hypoglycemia.

What happens? The insulinogenic function which is out of order does not shut off the secretion of insulin in time to prevent hypoglycemia as it does in the normal individual, and is thus constantly being overstimulated by the intake of carbohydrate all day long and produces more insulin to take care of that carbohydrate. The patient becomes worse and worse.

In cases like this the best thing to do is to restrict the carbohydrate to 100-120 gm. of carbohydrate a day, and to increase the protein and the fat to the desired number of calories. When you introduce a larger portion of fat into the food, the absorption is slowed down and thus there is not the same impact on the islands of Langerhans to liberate insulin as when the diet consists largely of carbohydrate which is a powerful stimulating factor to the insulinogenic function. Such a routine straightens out the hyperinsulinism if it is functional in nature (2). If it is anatomic, however, i.e., due to a tumor of the islands, then only a surgical intervention will correct it.

HUNGER IN UNDERNUTRITION

Occasionally we meet with a diabetic who has been scared to death when told of all the possible things that might happen to him. He was told right at the start of the early arteriosclerosis, the blindness due to hemorrhages in the eyes, hypertension, gangrene with its subsequent amputation of a leg or both legs, of intercapillary glomerulosclerosis, of the coma in which he may die, the "insulin shock," a bad pyschological term for an insulin reaction which simply scares the patient out of his wits, etc. Is it any wonder that such a patient is scared, scared of food and everything else? He eats but sparingly, takes an inadequate number of calories for his nutrition and he goes down and down. Always the fear of everything.

Here it is not the patient at fault but the physician who approached the problem in a most unwise and brutal manner. And it is no small job to change such a patient's thinking once it is ingrained. One must use wisdom in handling various types of patients and prevent such occurrences.

HUNGER IN HYPERTHYROIDISM

Hyperthyroid patients as a rule are always hungry and eat a lot to compensate for their loss of weight due to the increase of their metabolism. This is but natural. They usually crave sweets and sour things. Because of their overeating plus the overactivity of the thyroid gland, and the moderate ketosis which accompanies it, many develop frank diabetes. The incidence of permanent diabetes in hyperthyroidism in a series of 9000 cases I followed up (3) over a period of 10 years, showed two times the incidence of diabetes at large, namely 2.3 per cent. To counteract hunger in hyperthyroidism we need to use high caloric diets. If a patient with hyperthyroidism has an elevated blood sugar, we must use an adequate amount of insulin to control the hyperglycemia. This procedure saves many who without such protection, would become permanent diabetics. These patients are hungry during hyperthyroidism for the simple reason that they carry often hyperglycemia and are not burning up the large diet they took, but are excreting considerable amounts of sugar via the urine. In other words, they are not metabolizing the calories they take in. This is a physiological hunger, due to diminished utilization of food. Toxemias of all kinds block the action of insulin. It is likely due to this factor that we find hyperglycemia so often in cases of hyperthyroidism. In 1932 (3) I reported 6.88 per cent of abnormal hyperglycemia found in 9000 cases of hyperthyroidism and 19 per cent of glycosuria found in a series of 100 cases.

HUNGER FROM CHRONIC DIARRHEA

Hunger in diarrheas is due to the fact that food passes too rapidly through the gastrointestinal tract and has no chance of being properly and fully utilized. Thus, such a patient may be taking in an ample supply of calories, but the body receives benefit from only a portion of these calories and hunger results. This, of course, is a medical problem: correct the diarrhea and bring about proper utilization of the food taken.

HUNGER IN THE OBESE WHILE REDUCING

Obese patients are obese for the simple reason that they have been taking in too many calories a day, more than the body can utilize, the balance going into fat which increases the weight. Such patients "just love to eat" and they show it. I have carved a fat man for my office, and the legend under it says: "No one ever got fat by eating too little." I have noticed that the obese patients especially take a good notice of it. It is a gentle way of stating a fact.

When such a patient goes on a low caloric diet, he feels quite miserable. Of a hundred patients who start on reducing diets, not more than 3 to 5 will finish. I have even had such patients ask me for pills that would increase their "will-power." Tht means—failure. Yet those who succeed in reducing down to somewhere near normal weight never go back to over-eating, for they realize how much better they feel; how much more energy they have; and how much better they look; to say nothing about the penalties which go with obesity that they need no longer dread.

After a time on a low caloric diet, the feeling of misery ceases and the patient, once he has his weight down, can carefully raise his diet and yet maintain a normal weight. This is a point which should be emphasized to such patients for it is their final reward.

SOME EXPERIMENTS ON MYSELF

On doing repeated glucose tolerance tests on myself, for experimental purposes, I have experienced the hunger that we have been discussing, at about the third hour after the intake of 100 gm. of glucose, when the blood sugar has dropped to 40 or even 30 mg. per cent. This was an excruciating hunger which is hard to describe. One just feels that he has to have something to eat or perish. At such a time one will eat anything and everything he can lay his hands on. I stuck it out, however, always to the end of the test, the 4th hour, but the remembrance of that hunger is still very vivid in my mind. I surely know what true hypoglycemia means.

Then there is another occurrence of hunger which

I have experienced personally. For some 15 years now, I have experienced, usually in the middle of the afternoon, attacks of extreme hunger, nervousness and profuse perspiration all over the body. This used to happen two or three times a year. I believe this is an insulin reaction due to excessive endogenous insulin causing a hypoglycemia. I have not taken insulin at any time so that I attributed it to "endogenous, accidental hyperinsulinism." Checking my blood sugars during these attacks, the blood sugar was invariably 32, 34, 36 mg. per cent. A few chocolates or some sweets in any form would relieve these attacks within 10 minutes. Checking the blood sugar again, i.e., within 15 minutes after taking the carbohydrate, the blood sugar had risen to normal and the hunger ceased. During the attack I experienced extreme hunger, together with other classic symptoms of hypoglycemia. Hypoglycemia almost invariably produces hunger and it is that sort of thing that happens occasionally to diabetics who are taking insulin if the insulin is not closely adjusted. Or it can happen when the injected insulin one day is not fully absorbed and a full dosage is given the next morning, in which case we get some overlapping of the action of the insulin so that a well adjusted dosage becomes an overdosage.

However, as can be seen from the preceding, hypoglycemia can happen to a non-diabetic, one not taking insulin; especially when something goes wrong with the regulatory mechanism controlling endogenous insulin secretion. I am citing this personal experience for the simple reason that there must be many others in the world who have gone through similar experiences. We must bear it in mind when confronted with such a clinical manifestation. Even non-diabetics, CAN have an insulin reaction!

I might cite experiences such as appeared in Reader's Digest, Oct., '48, p. 109, with the heading: "Keep Off the Grass."

Take the jockey: There was "Balding Williams who had the bones for a man 135-140 pounds. Yet he was required each day to make weights of 110-115 pounds, including his saddle and clothes. This of course meant rigid dieting. His breakfast—nothing. Lunch—a carrot or a tomato. Dinner—lamb chops, broiled, always broiled, meat and salad, vegetables and coffee.

"Sometimes we get so hungry we can't stand it anymore. We sit down and have pastry, and gravy, and bread, and fried potatoes and cheese and pork and candy. And we gulp it down with a lot of water. All the things we've been craving for months, years sometimes. We just stuff it down. Then we bring it all up before it gets digested. Like the Romans."

This resembles the picture of a diabetic who has been kept on a rigid diet for a long time. The accumulation of craving for "real food" finally reaches such a point that he can no longer endure the rigid routine and he breaks down under it and does what the jockey did all except the regurgitation. This of course applies mostly to those diabetics who are kept on unreasonably low diets. I had one patient in the early twenties, a young woman who was on an 1800 calorie diet. The family was so worked up about her that they watched her every step, locked the food so that she could not possibly get at it, treating her like a criminal. It was no wonder that one day they found her dead, she having put a bullet through her head rather than to live the life that she thought was before her.

To come back to our jockey. In one race, he was seen jerking his head as he sat on the horse in the race, finally falling off the horse and the jockey "was seen down on his hands and knees in the fresh, wet clover of the infield, his face buried in the greenery and his head and shoulders bouncing up and down, cowlike. One of the stewards shouted: "Get him out of there! He is eating grass!"

Hunger is a potent factor. It can be brought on either by: a. insufficient food, b. adequate food but inadequate utilization of that food, namely inadequate insulin dosage, c. hypoglycemia caused by too much or improperly adjusted insulin. In any of these three conditions the same final picture results and leads to extreme hunger and craving for food, resulting finally in the gorging of food, failure in the treatment of diabetes. The psychological as well as the physiological factors are present and it shows that good judgment, based on adequate laboratory findings must be used if we are to eliminate such catastrophies.

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A NEW APPROACH TO THE ETIOLOGY AND MANAGEMENT OF CONSTIPATION

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DIARRHEA and/or constipation may be the result of, or associated with organic disease within or outside the gastrointestinal tract, or from functional disturbances associated with psychosomatic and psychotic conditions. Failure to respond promptly to the physiological call of nature to defecation, irregular habits of defecation, improper diet, high pressure living, colon consciousness and insufficient fluid intake are the common background of constipation.

In nutritional disturbances, overweight, old age, chronic wasting diseases, etc., there is weakness and/or

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suppression of the activity of the musculature of the intestinal tract which causes stagnation of the contents, infrequency of the bowel movements, and is referred to, as atonic constipation. On the other hand, in certain individuals who are irritable due to high pressure living, and emotional disturbances or psychosomatic factors, the colon becomes irritable and spastic, causing a delay in the onward movements, and failure of the purposeless contractions attempting evacuation, resulting in spastic colitis (1).

When the rectum is full, a physiological call is initiated and the reflex impulses for the evacuation of the bowel are set in action. If this call is inhibited, the rectum adjusts itself to the increased bulk, and therefore the desire to have a bowel movement ceases. With the stagnation of the bowel contents, there is further absorption of water, and in turn the feces become very hard and difficult to expel. The distention of the sigmoid and rectum results in further sluggishness of the movements through the thinning out and atony of the intestinal musculature. If adequate emptying of the bowel is to be maintained, the physiological call should not be inhibited or postponed because it will lead to bad habits. The daily evacuation of the bowel should be a part of the training from early childhood. In some individuals, there is an inherent nature of an undue absorption of the water from the colon, thus giving rise to hard stools (2).

A diet rich in carbohydrates and vegetables promotes the overgrowth of the aciduric or saccharolytic bacteria, giving rise to acid end products, and the excess of cellulose furnishes an adequate bulk, leading to loose or normal bowel movements. High protein diet suppresses the saccharolytic group and promotes the overgrowth of the proteolytic bacteria. On such a diet, the intestinal bulk is small and may result in infrequency of movements (3).

In disturbances of the gastrointestinal tract, the normal intestinal bacteria have shown quite a wide range of variation. In chronic ulcerative colitis, the normal intestinal bacteria were increased 85 fold while the coliform organisms were increased 50 fold (4); in chronic amebiasis, the total bacteria were increased 40 fold and the coliform increased 20 fold (5); in transplantations of the ureters into the sigmoid, the total was increased 10 fold while the coliform 5 fold (6); and in pyorrhea alveolaris the total was increased 61.7 fold and the coliform 37 fold (7).

Chronic constipation of functional origin reduces the general physical tone, leading to physical and mental sluggishness and fatigue, secondary colitis, hemorrhoids, fissures, and may act as a focus of infection. A thorough history and physical examination is very important in all cases of constipation to rule out organic disease. Past history is important in reference to habits, training evacuations, diet, use of laxatives, exercise, shigellosis or amebiasis, and other gastrointestinal and systemic disorders.

Clinical Studies

This study included 33 cases whose age ranged from 21 to 62 years. Thorough physical examination, complete history and in some cases G I series, barium enema and electrocardiograms ruled out the presence of organic disease, however two patients were apparently suffering of asymptomatic amebiasis since the cysts of *Endameba histolytica* were found in routine stool examination.

Although the chief complaint was chronic constipation, these patients also presented any combination of the following symptoms: strain on defecation, fullness in the rectum or epigastrium, anorexia, indigestion, bloating, discomfort or heaviness after meals, belching, regurgitation, flatulence, vague abdominal pains, headache, malaise, chronic fatigue, lack of energy and ambition, arthralgia or myalgia, foul breath, coated tongue, colon consciousness, hemorrhoids, fissures, rectal prolapse, focal infections, palpable liver, underweight, etc.

Laboratory Studies

Warm stools were examined for ameba, cysts and ova of parasites by direct examination in saline or Lugol's solution. Zinc floatation method was used for the concentration of the cysts of ameba. The stools were cultured in modified Boeck and Drbohlov medium for *E. histolytica.*

For the isolation of Salmonella, Shigella and *Streptococcus fecalis,* the stools were streaked on eosin methylene blue and S S plates. For the bacterial counts (total and coliform), the stools were kept in the ice box, and the count was made by Henderson Seneca technic (8).

Blood was collected for the erythrocyte sedimentation rate (Wintrobe), and white and red blood cell counts.

In suspicious cases, G. I. series, barium enema and sigmoidoscopic examinations were made to rule out pathology.

Laboratory Findings

Cysts of *E. histolytica* were found in two cases (Nos. 21 and 29), for which they were given the specific antiamebic treatment. *Streptococcus fecalis* was isolated in 17 cases (51.5%), but no Shigella-Salmonella were cultured.

The white cell count was normal in all cases except in three who had a leucocytosis of more than 10,000 w b c per cmm. The red blood cell count was less than 4.5 million/cmm in 14 cases, with two patients having less than 4 million. The sedimentation rate ranged from 2-48 mm/hr. In 14 patients it was more than 15 mm/hr; in 11 it was more than 20 mm/hr; in 5 more than 30 mm/hr; and in two, it was over 35 mm/hr.

The average number of bacteria in the stools of a normal individual with normal bowel movements was 165 billion bacteria per gram of wet feces, 123 billion of which were coliform organisms (8). The bacterial counts were increased in all cases except in case No. 14 who had a normal count. The highest count was 46,000 billion total bacteria, 44,000 billion of which were coliform organisms (case No. 13). The average increase was 32 fold for the total bacteria, and 19.4 for coliform organisms, as compared with the normal.

Management

Training and education of the patient, particularly in early childhood are very important in the prevention of constipation. The diet should be well balanced.

TABLE I. LABORATORY FINDINGS IN PATIENTS SUFFERING OF CHRONIC CONSTIPATION

	Name	*Age*	*Blood Count* R.B.C.	W.B.C.	*E S R* mm/hr.	*Bacterial Count in Billion* Total	Coliform	*Other Findings*
1.	P.H.	22				1,110	130	
2.	J.B.	21				12,160	6,640	
3.	S.H.	51	4.87	9,350	48			
4.	G.G.	60				375	295	
5.	S.T.	45	4.42	8,100	20	15,360	2,200	
6.	H.S.	48	4.3	7,950	35	3,000	1,200	S. fecalis
7.	L.B.	43	3.81	8,500	26	3,600	1,800	
8.	R.K.	41	4.1	8,150	15	5,280	2,200	
9.	T.D.	29	4.0	5,450	10	4,400	2,400	S. fecalis
10.	E.L.	32	5.0	6,200	5	1,280	550	
11.	A.L.	57	5.0	4,850	30	1,310	700	S. fecalis
12.	B.S.	21	4.25	9,350	8	7,000	5,100	S. fecalis
13.	M.F.	46	4.75	8,100	22	46,600	44,000	S. fecalis
14.	C.C.	40	4.8	6,500	13	120	103	S. fecalis
15.	A.T.	24	4.37	5,400	18	18,600	15,600	S. fecalis
16.	H.G.	36	4.76	8,500	2	2,100	1,100	
17.	H.S.	29	4.15	9,450	35	2,100	1,100	
18.	G.M.	27	4.97	8,450	13	370	170	S. fecalis
19.	V.T.	64				1,500	820	
20.	A.M.	43	5.5	8,100	13	2,200	1,100	S. fecalis
21.	A.D.	29	4.9	9,300	12	3,100	1,210	S. fecalis E. histolytica
22.	P.D.	62	5.3	7,650	13	4,000	2,800	S. fecalis
23.	H.P.	45	4.15	6,560	8	2,900	1,400	S. fecalis
24.	M.S.	54	4.3	10,250	30	4,200	2,100	
25.	C.S.	24	4.25	10,400	18	1,900	800	S. fecalis
26.	B.L.	38				4,500	2,010	S. fecalis
27.	R.L.	32				1,850	1,700	S. fecalis
28.	Y.O.	45						
29.	S.M.	28	4.06	9,400	26	3,100	1,010	E. histolytica
30.	G.T.	36	3.8	6,450	30	2,410	980	
31.	A.K.	56	4.1	6,400	32	4,100	1,850	S. fecalis
32.	M.K.	58		9,000	37	2,900	1,100	S. fecalis
33.	H.S.	44	5.1	10,100	15	1,850	800	
			Fold increase (average)		Total bacteria Coliform	32 19.4		

Laxatives may have their place, but the irritating and oily ones should not be used over a long period of time. Pathology if discovered should be corrected. Routine blood counts and sedimentation tests should be done. The stools should be examined for pathogenic parasites and bacteria. Bacterial counts should be done on the stools to determine the number of normal intestinal bacteria per gram of wet feces. Psychosomatic factors and colon consciousness should be corrected, and high pressure living should be normalized. Physiological call to defecation should not be inhibited or postponed.

In view of the increase in the number of normal intestinal bacteria, and/or the presence of *Streptococcus fecalis*, these individuals were put on subtherapeutic doses of antibacterial agents, namely non-absorbable sulfonamide, such as phthalylsulfacetamide (Thalamyd Schering). Large or therapeutic doses markedly reduced the intestinal flora, and if used over a long period of time, interfered with the synthesis of vitamins by the intestinal bacteria, and could result in superimposed overgrowth of *Candida albicans, Micrococcus pyogenes, Proteus vulgaris, Pseudomonas aeruginosa,* etc.

Phthalylsulfacetamide was used in one to two gram daily doses for one to two weeks, and then reduced to one gram daily for a period of one to two months. Thereafter, it was repeated to control constipation, using the same dosage. The antibacterial therapy reduced or modified the intestinal bacteria, and got rid of *Streptococcus fecalis*. They were also given multivitamins to restore the vitamin intake and correct the anemia and restore the general vitality. Yogurt or butter milk was added to the diet to avoid or prevent the side effects of the antibacterial treatment, and to restore the normal intestinal bacteria by replacing the pretreatment bacteria with aciduric organisms. Yogurt is the result of the growth in the milk of *Lactobacillus bulgaricus, Streptococcus acidi lactis* and *Thermobacterium yogourti*. It also possesses antibacterial properties (9). Butter milk is inferior to yogurt. Unfortunately, *L. bulgaricus* can not be implanted in the colon for a long time, therefore the patients should constantly eat yogurt. A word of caution concerning dried preparations or lyophilized forms of lactobacilli. In such preparations, the survival time of lactobacilli is very short. The cheapest and best form of lactobacilli is yogurt.

The mild anemia (14 cases), leucocytosis (3 cases) and increased sedimentation rate (14 cases) indicate that constipation may cause disturbances in the physiological processes. It is not yet known if these changes could result from the action of toxic metabolites absorbed from the colon. Metschnikoff (10) called it intestinal autointoxication.

There is no reference in the literature to indicate that *Streptococcus fecalis* (Lancefield Group D) is pathogenic in the colon. Bargen's diplostreptococcus (11) which causes "thrombo-ulcerative" colitis is probably not related to *S. fecalis*. On the other hand *S. fecalis* differs from *Streptococcus lactis* by being thermostable at 60 degrees C for 30 minutes. If and when S. fecalis invades the tissues outside the bowel, it becomes highly pathogenic and causes serious troubles. It may be feasible that *S. fecalis* possesses low grade pathogenic effect on the colon, and eventually may result in atony of musculature leading to constipation.

It can be reasoned that there is a normal or physiological balance between the nonpathogenic bacteria in the colon, and the colonic mucosa, thus preventing the invasion of the bowel wall by the bacteria, and preventing the absorption of the toxic bacterial metabolites because of the high threshold of absorption for these compounds. If there is an increase in the number of bacteria, this balance could be thrown out of equilibrium due to the increased production of these products which pass the threshold level of absorption. Moreover, the increase in the number of bacteria might increase the chances of permeation through or invasion of the wall of the colon.

The combined antibacterial, yogurt or buttermilk (lactobacilli) and vitamin therapy has given promising results in the reduction in the number of intestinal bacteria and modification of the flora, thus helping to restore the normal bowel movements. A more complete report will be made at a later date, including the use of nonabsorbable antibiotics.

Summary and Conclusion

1. In chronic constipation the normal intestinal bacteria was increased 32 fold and the coliform 19.4 fold. In 14 of 33 cases there was a mild secondary anemia and increased sedimentation rate.

2. Promising results were obtained by using a combined antibacterial (phthalylsulfacetamide) and yogurt or butter milk therapy through the reduction and/or modification of the intestinal flora.

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THE CAPILLARY SYNDROME IN HEMORRHAGIC CYSTITIS THERAPEUTIC EVALUATION OF BIO-FLAVONOIDS*

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IN HIS classic work, Valy Menkin (1) defined and interpreted the mechanism of inflammation. He pointed out that an increased capillary fragility and subsequent capillary bleeding leads to the injury of cells in the inflamed tissue. As a result of this cellular injury and destruction, certain toxic substances are liberated, which in their turn augment capillary permeability and aggravate the process of inflammation. He identified these substances as "leukotaxine" or "LPF" (leukocytosis-promoting factor). By his studies, Menkin was able to explain the role of the capillary syndrome, a term first introduced by Eppinger (2) in connection with the protein leakage into the tissues which occurs in inflammation. Sokoloff *et al* (3) in their investigations on bacterial polysaccharides and their effects on capillary fragility, discovered that certain bio-flavonoids, otherwise known as citrus vitamin P, drastically reduced capillary permeability and minimized the Schwartzman phenomenon.

The previous work of Armentano *et al* (4), Bacharach *et al* (5), Scarborough (6), Griffith and Lindauer (7), Sokoloff and Eddy (8), and others established the specific activity of bio-flavonoids in regard to capillary fragility phenomena. The usefulness of this compound in increased capillary fragility, induced by bacterial infections, was stressed by these investigators. More recently, Biskind and Martin (9, 10) reported the therapeutic value of bio-flavonoids in upper-respiratory infections and attributed the salutary effect of these substances to their activity in reducing capillary permeability. Sokoloff (11) investigated the effect of bio-flavonoids in virus A influenza and confirmed the beneficial effect on the course of the infection reported by Biskind and Martin. Payne (12) and Jones and Croce (13) reported prompt arrest of bleeding in tuberculous hemoptysis and enhancement of the resorptive process with bio-flavonoid therapy.

In trigonitis and cystitis, the mucous membrane of the bladder is, as a rule, inflamed, and the self-disinfectory property of it considerably reduced. This is particularly so when a localized capillary syndrome is present and capillary bleeding is observed.

The present report, which is of a preliminary nature, covers 19 cases of hemorrhagic trigonitis and cystitis treated with bio-flavonoids. The preparation known as C.V.P.**, or citrus vitamin P, was administered in a dosage of 2 or 3 capsules, 100 mg. per capsule, at 8 A.M., 12, 4 P.M. and 8 P.M. for 3 or 4 days. Seven cases of cystitis treated with Gantrisin***, 6-8 tablets daily, 0.5 gm. per tablet, served as a comparison series.

The following case histories may be given as typical as far as the response of the infection to these therapies is concerned. All cases were examined and diagnosed by cystoscopy without benefit of local anesthesia.

BIO-FLAVONOIDS

S. H., white, female, age 47, no children. Examined on May 24, 1954.

Examination: Urine, microscopically: Numerous red blood cells and pus cells. Culture: *Escherichia coli* and *Pseudomonas aeruginosa.*

A pin-point ulcer near the right ureteral orifice, on cystoscopy.

Diagnosis: Hemorrhagic, ulcerative trigonitis and cystitis.

Treatment: C.V.P., 2 capsules (200 mg.) at 8-12-4-8 P.M. Started on May 25, 1954. No local treatment was employed.

May 27, 1954: Tenesmus, frequency and urgency minimal. Urine microscopically: several red blood cells per high power field.

May 31, 1954: Clinically well. Urine microscopically: occasional red blood cells, no pus cells or casts. Culture (48 hours) negative. No side effects.

E. M., white, female, age 42, two children. Examined on May 24, 1954.

Examination: Urine, microscopically: Numerous red blood cells and pus cells. Culture: *Escherichia coli* and *Pseudomonas aeruginosa.*

Diagnosis: Hemorrhagic trigonitis and cystitis.

Treatment: C.V.P., 2 capsules (200 mg.) at 8-12-4-8 P.M. Started on May 25, 1954. No other medications, no local treatment.

May 27, 1954: Urine microscopically: grossly clear. A few red blood cells. Clinically feels well.

May 31, 1954: Urine microscopically: no red blood cells or pus cells. Culture (48 hours) negative. Clinically cured. No side effects.

A. H., white, female, age 64, one child. Examined on July 27, 1954.

Examination: Urine, microscopically: Numerous pus cells, numerous red blood cells, a few pseudocasts. Culture: *Escherichia coli* and *Staphylococcus viridans.*

*Aided by a grant from the Marcia Tucker Foundation.

**The flavonoid preparation used in this study was C.V.P.®, a mixture of equal parts of whole water-soluble natural citrus flavonoids, and ascorbic acid. Each capsule contains flavonoids, 100 mg. and ascorbic acid 100 mg. Through this paper the dosage refers to the flavonoid component only (1 capsule = 100 mg.). C.V.P. is manufactured by U. S. Vitamin Corporation.

Editor's Note: This article is presented because of its nutritional interest, in spite of the fact that it does not pertain to gastroenterology.

Submitted, Feb. 8, 1955.

***Gantrisin, a sulfa preparation, is manufactured by Hoffmann-La Roche.

Diagnosis: Hemorrhagic trigonitis and cystitis.

Treatment: C.V.P., 3 capsules (300 mg.) at 8-12-4-8 P.M. Started on July 27, 1954. No other medication.

July 29, 1954: Clinically well. Urine microscopically: occasional pus cells; few red blood cells.

August 3, 1954: Clinically cured. No side effects. Urine microscopically: negative, no pus cells, no red blood cells. Culture: negative.

GANTRISIN

A. S., white, female, age 44, two children. Examined on April 12, 1954.

Examination: Urine, microscopically: Numerous red blood cells and pus cells. Culture: *Escherichia coli.*

Diagnosis: Hemorrhagic trigonitis and cystitis.

Treatment: Gantrisin, 2 tablets (1.0 gm.) at 8-12-4-8 P.M. Started on April 12, 1954. Local instillation: Silver proteinate, 20 cc.

April 15, 1954: Symptoms only moderately lessened. Still considerable urgency and frequency. Silver proteinate instilled in bladder.

April 17, 1954: No change in the patient's condition.

April 20, 1954: Condition much improved. Gantrisin discontinued. Silver proteinate instilled in bladder.

April 23, 1954: Culture: negative. Patient well. Side effect: minimal nausea.

A. N., white, female, age 66, eight children. Examined on July 6, 1954.

Examination: Urine microscopically: Myriads of pus cells. Numerous red blood cells. Culture: *Escherichia coli.*

Diagnosis: Hemorrhagic, ulcerative trigonitis and cystitis. Cystourethrocele (Grade II).

Treatment: Gantrisin, 3 tablets (1.5 gm.) at 8-12-4-8 P.M. Started on July 6, 1954.

July 9, 1954: Essentially no clinical improvement. Microscopically, considerable number of pus cells, numerous red blood cells.

July 12, 1954: Clinically much improved. Tenesmus, frequency minimal. Microscopically, few pus cells, few red blood cells.

July 19, 1954: Clinically well. Culture: negative after 48 hours. Side effect: considerable gastrointestinal disturbances.

I. S., white, female, age 39, no children. Examined on July 13, 1954.

Examination: Urine, microscopically: Numerous red blood cells and pus cells. Culture (48 hours): *Escherichia coli* and *Pseudomonas aeruginosa.*

Diagnosis: Hemorrhagic trigonitis and cystitis.

Treatment: Gantrisin, 2 tablets (1.0 gm.) at 8-12-4-8 P.M. Started on July 13, 1954. No local treatment.

July 16, 1954: Clinically, some improvement. Microscopically, several pus cells and red blood cells.

July 20, 1954: Clinically well. Microscopically, occasional pus cells and red blood cells. Culture: negative in 48 hours. Gantrisin stopped. Side effect: nausea.

July 27, 1954: Clinically well.

The following table summarizes our observations:

TABLE

COMPARATIVE EFFECT OF BIO-FLAVONOIDS AND GANTRISIN ON ULCERATIVE CYSTITIS

Medication No. of cases	Sex	Total Dosage, Average	Clinical Relief	Bacteriol. findings Average	Side-Effects
19 cases, treated with bio-flavonoids	Females	6.2 gm.	3-4 days	Return to normal, av. 5 days	NONE
7 cases, treated with Gantrisin	Females	35 gm.	5-7 days	Return to normal, av. 5 days	Frequent nausea, gastric irritability

Analysis of the figures presented in the table indicates a favorable response of the patients with hemorrhagic cystitis to the bio-flavonoid therapy as compared with gantrisin. In both series, the return of bacterial flora to normal and the disappearance of pus cells and red blood cells took place within five days, average. The clinical improvement appeared to proceed somewhat faster in the cases treated with bio-flavonoids than in those receiving Gantrisin. However, the difference in this respect was not significant. In general, the well-being of the first group of patients (on bio-flavonoids) was more pronounced than in the second group (on Gantrisin). There was no side effect from bio-flavonoid therapy, while Gantrisin often induced nausea and gastric irritability.

COMMENT

The limited number of cases treated by us with bio-flavonoids obliged us to make the conclusions with some reservation. Yet there was an intriguing phe-

nomenon, revealed by this study, that an anti-inflammatory substance, as is the case of bio-flavonoids, may produce similar therapeutic effects on hemorrhagic cystitis, as the sulfa preparation, Gantrisin, which has a wide-spectrum of antibacterial activity. This phenomenon suggests the important role which an injury to the capillary system and the subsequent inflammatory processes might play in promoting and aggravating bacterial infections. The fact that bio-flavonoids are antagonistic in their action to hyaluronidase and that they exert a salutary effect in viral infections as reported by other investigators (9, 10, 11) gives additional weight to the potential therapeutic value of bio-flavonoids as anti-inflammatory agents in bacterial and viral diseases.

SUMMARY

Nineteen cases of hemorrhagic cystitis and trigonitis were treated with bio-flavonoids, otherwise known as citrus vitamin P. (C.V.P.).

The results of this therapy compare favorably with those of the seven cases of hemorrhagic cystitis and trigonitis treated with Gantrisin, a sulfa preparation.

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ATHEROSCLEROSIS: OVERNUTRITION OR MALNUTRITION?

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ATHEROSCLEROSIS is a pathological process of the intima of the aorta, coronary and other large arteries characterized by lipid deposits and subsequent inflammatory and degenerative processes. Atherosclerosis and coronary heart disease is the main cause of death in the Western world.

The outstanding facts, now widely, but by no means generally accepted, are: 1) In the Western world heart disease is constantly increasing. 2) Atherosclerosis and heart disease are related, although the severity of the sclerosis is not a correct criterion for the severity of the heart disease. 3) Western physicians (1, 2) have always confirmed that angina pectoris, coronary thrombosis with myocardial infarction, senile gangrene, inflammatory diseases of the veins, widely ulcerated lesions of the intima and thrombophlebitis of the femoral vein are decidedly rare in Eastern countries. 4) The Mediterranean countries and large parts of South America suffer less than North America, Great Britain, Australia or Holland. 5) Atherosclerosis is induced by a disturbed lipid metabolism. 6) The composition of serum lipids can be influenced by nutrition. 7) Food is of predominant importance in the development of atherosclerosis.

Increasing knowledge has been able to exterminate, with the exception of small isolated instances, the classic forms of nutritional disease and it is suggested that the attention of nutritionists should now be focused to the main food problem of our time: overnutrition.

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DIETARY EXCESS OR DIETARY DEFICIENCY?

Most current research is based on the hypothesis that the Western food contains factors toxic to the arteries. This hypothesis suggests that these factors are not present, or not present to such a dangerous level, in Eastern foods.

The deficiency theory depends on the hypothesis that Eastern food contains preventive factors, not present or not available in adequate amount, in Western foods. The deficiency theory has not yet been consistently tested by the leading scientists, working on the relationship between food and atherosclerosis.

THE INTOXICATION THEORY

The early recognition that lipids, chiefly cholesterol, are deposited in diseased vessel walls has suggested that an excess of cholesterol in the diet causes atherosclerosis. Others have rejected the idea and have suspected the fat content or the calorie content of food. The intoxication concept has led to the determination of certain blood lipids for diagnostic purposes. Cholesterol, the quantity of certain low density lipoprotein fractions, chylomicron counts, serum turbidity, cholesterol/lipid phosphorus ratios have been used to designate the atherosclerotic state, but none of these

techniques yields a specific picture of the condition of the cardiovascular system. The data of patients and normals overlap considerably. Furthermore the maximum tolerance varies with age, sex, race, food habits, diet, mental and physical stress, etc.

The hypothesis that atherosclerosis is caused by some form of overnutrition invariably leads to dietary restrictions for patients. These restrictions are often, but not consistently, followed by a drop of serum lipid values. The rigid diets, used by physicians to obtain clear-cut decrease of serum lipid values, have apparent drawbacks, however. Cholesterol-free, fat-free or undercaloric diets are impossible to maintain for long periods; discontinuance of the diets restores pre-experimental conditions, so that the effect is lost. Furthermore, not all patients are overnourished or obese, nor can obesity be always ascribed to pure overnutrition. All these dietary restrictions have one thing in common: they are drawn up on the intoxication concept and are wrongly supposed to be a true copy of non-atherogenic eastern food. Apparently the west opposes the idea of deficiencies in the diet. There is no evidence that eastern peoples might survive or feel well on similar inadequate food. Nor is there any evidence that atherosclerosis or heart disease can be indefinitely prevented by permanent undernutrition, by the avoidance of fat or of all animal products.

THE INTOXICATION BY DIETARY CHOLESTEROL

The underlying line of thought is: cholesterol in food—cholesterol in blood—cholesterol in the artery wall—coronary disease. It implies that people living from the yield of herds, fishing and hunting are having, and our ancestors in the Western countries (who lived on butter and lard as the main source of fat) have had much more coronary heart disease than the present consumers of vegetable margarine and shortenings. It also implies that vegetarians are not sensitive to the disease. It does not explain why such a poisonous compound is synthesized by all animals in larger amount than it is consumed in an average diet. As mother's milk contains cholesterol and the embryo developing in the egg encounters 250 mg. of cholesterol for prenatal consumption (a percentage high enough to induce experimental atherosclerosis in chickens), it seems unreasonable to assume that the concentration of cholesterol, present in animal food, can be the main etiological factor in atherosclerosis.

The cholesterol intoxication theory finds support in nutritional experiments. In certain animals, notably the chicken and the rabbit, lesions of the vessels can be increased by feeding unphysiological amounts of cholesterol. In some other animals it is very difficult to cause lesions by feeding cholesterol, unless the experiment is combined with suppression of function of the thyroid gland or the concurrent administration of large amounts of vitamin D.

The influence of animal and vegetable food on the blood cholesterol level of healthy humans has been studied by Groen *et al* (3). They used diets containing 1,300 and 900 mg. of cholesterol respectively and found a good correlation between diet and serum cholesterol levels. But the diets used were so different in all other respects (phospholipids, composition of fatty acids, inositol, choline, composition of proteins), that it would be premature to ascribe the fluctuations of serum cholesterol to the cholesterol content of the diet. Furthermore the serum cholesterol levels were greatly influenced by stress factors independent of the diet. On the vegetable diets, used by Groen, the test subjects did not feel well and suffered from pronounced psychical disturbances. Similar studies do not indicate whether the fluctuations in serum cholesterol are a physiological or a pathological phenomenon.

THE FAT INTOXICATION

This concept suspects the percentage of fat calories in the diet. The underlying line of thought is: fat in food—cholesterol in blood—cholesterol in the artery wall—coronary disease. There is no experimental evidence for this point of view, for fat feeding does not cause atheromatosis in experimental animals. It is not made clear by what mechanism the dietary fat is converted into cholesterol and how we should control the endogenous synthesis of both cholesterol and fat from carbohydrate metabolites. The evidence is drawn from statistics, comparing: 1) the incidence of atherosclerosis and its consequences. 2) the blood cholesterol levels. 3) the average fat percentage, consumed in the Western, Eastern and Mediterranean countries.

The influence of dietary fat on the serum cholesterol level is studied by various authors. Severe reduction of dietary fat reduces serum cholesterol and addition of fat to a fat-free diet increases the cholesterol level, but as fatty acids are at least partly esterified to serum cholesterol, these fluctuations may be explained as a physiological participation of cholesterol in fat transportation. Keys (4) claims that vegetable and animal fats have the same effect and that addition of cholesterol to the diet has no influence on the serum cholesterol level. Kinsell (5) *et al.* and Beveridge (6) *et al.* report that isocaloric substitution of plant for animal fat in the diet of patients may result in a marked lowering of serum cholesterol. But this effect was not due to the cholesterol of the animal fat, as addition of large amounts of cholesterol to the vegetable fat did not restore serum cholesterol to its previous level.

From these studies it can be concluded that the serum cholesterol level is dominated by the fatty acid pattern of the diet rather than by the cholesterol content. Yet it seems not justified to supplement human food with large amounts of cholesterol, as some investigators have done. Apparently, exogenous cholesterol hardly influences the serum cholesterol level, but it may well initiate atheromatosis.

THE CALORIC INTOXICATION

The difficulties in understanding the fat intoxication theory has led to the conception of intoxication by overcaloric diets, irrespective of the quality of the food. The underlying line of thought is: too many calories—cholesterol in blood—cholesterol in the artery wall—coronary disease. No explanation of the mechanism is available and experimental animals do not overeat, unless the hypothalamic center is damaged, but this experimental hyperphagia is not consistently followed by coronary disease.

In rabbits on a high cholesterol intake caloric retriction not only does not give any protection against vascular disease, but seems to enhance both the hyperlipemia and the atherosclerosis (6, 7).

The theory of overnutrition leads to odd consequences. A theoretical diet in which all (known and unknown) nutrients are present in optimal amounts would be able to cause the most frequent and the most fatal of all nutritional diseases by exceeding a certain (as yet unknown) caloric value. This conception must necessarily discourage future workers, as it *a priori* assumes that atherosclerosis is an inevitable consequence of the availability of food, irrespective of its quality. It concludes that humans (or perhaps the Western peoples only), unlike animals, can not control their appetite.

The theory of dietary intoxication has led to many conflicting nutritional conceptions and to little clinical success.

THE DEFICIENCY THEORY

The deficiency theory suggests the presence of preventive factors in the diet of Eastern peoples, which have been partly or entirely discarded from the Western food. A number of dietary factors may prevent the deposition of abnormal lipids in experimental animals.

Kánocz and László (8), as early as 1934, investigated the cholesterol-lecithin antagonism in the surviving vessel wall confirmed in the rabbit, fed on a natural diet. When 1% of cholesterol was added to the diet, the rabbits showed 1) a considerable increase of serum cholesterol, 2) a considerable increase of the ratio cholesterol/lecithin, 3) a 30-40% rise in blood pressure and 4) extensive aortic lesions. When the diet was supplemented with 1% cholesterol and 1% lecithin the rabbits showed 1) a considerable increase of serum cholesterol, 2) no increase or even a decrease of the ratio (by a disproportionate rise of the serum lecithin), 3) no increase in blood pressure and 4) entirely normal vessel walls. After sacrificing, the cholesterol/lecithin ratio of the artery wall itself was 2 (control), 7.5 (in the cholesterol-fed animals) and 1 (after cholesterol + lecithin feeding).

CHOLINE

Wilgram, Hartroft and Best (9) reported on lipid deposits in walls of coronary arteries and grossly evident sclerosis in young rats after short periods on a low-choline, high-fat diet. The diets contained no supplements of cholesterol and high levels of protein, but were relatively low in methionine. In all the choline-supplemented controls abnormalities were absent. In these experiments several fats were used. Beef fat and lard were more atherogenic than were coconut oil (80% C_8-C_{14} fatty acids) or corn oil (60% linoleic acid) (10).

Biochemically, oxidation of long-chain fatty acids is depressed in liver, kidney and heart slices of choline-deficient animals and in vivo administration of choline restores the ability of these organs to oxidize fatty acids at a high rate. (Arton) (11, 12). That choline, in the choline-deficient dog, is used for the synthesis of choline-containing phospholipids of liver was shown by diLuzio and Zilversmit (13).

INOSITOL

Ilka, Felch and Dotti (14) found that hypercholesterolemia and cholesterol-induced atherosclerosis in rabbits was checked by inositol.

Essential fatty acids. A fat-free diet in growing male rats resulted in consistent infiltration of fat in the liver cells and abnormal weights of hearts, kidneys (and brains). Definite effects of essential fatty acid deficiency were present before the appearance of skin lesions (Panos and Finerty) (15). Chemically the essential fatty acids are very abundant in all glycerophosphatides, whereas in animal tissue fat they are relatively rare.

Pantothenic acid prevents heart and kidney damage and fatty infiltrations in the liver in experimental animals (17). Chemically it is a constituent of coenzyme A and most of the cellular-bound pantothenate exists as coenzyme A or its deriatives. Biochemically coenzyme A is the catalyst, which effects the synthesis of lecithin from simple building blocks (18, 19) and it plays a fundamental role in both carbohydrate and fat metabolism.

Pyridoxine (vitamin B_6). Arterial lesions, remarkably like those of human atherosclerosis develop in monkeys, subjected to protracted pyridoxine deficiency (20, 21).

Vitamin B_{12}. Chick embryos from B_{12} deficient hens had fatty hearts, livers and kidneys. Injection of B_{12} in the hens or in the eggs prior to incubation prevented these abnormalities (22). Biochemically B_{12} effects the synthesis of choline from methionine.

Magnesium. Calves fed a magnesium-deficient diet were found to have hemorrhagic areas in the heart, in the large blood vessels and in the kidneys. Histological examination showed thrombus formation associated with necrosis and other changes in the heart (23). Magnesium influences chylomicrons (25) and serum cholesterol levels (24). Biochemically magnesium is an activator or constituent of several enzymes, including coenzyme A.

NUTRITIONAL IMBALANCE IN WESTERN STAPLE FOOD

Progressive industrialization is rapidly changing our food. Western food has often undergone some form of stabilization, fractionation or chemical change in order to interfere with the metabolism of the food itself. Phosphatides, phytin, trace minerals and vitamins are for the greater part discarded from our main sources of carbohydrates and entirely discarded from our main sources of vegetable oil and fats. In the production of refined cereals (wheat flour, corn starch, table rice) the endosperm is carefully separated from germ and bran and this process removes most of the essential nutrients, including the greater part of all phosphorus compounds, minerals and vitamins. In commercial wheat grading white colour and low ash content are a measure for salability. American low extraction flours are "enriched" with two commercially available vitamins, but the loss of other B-vitamins, phosphorus compounds, trace minerals and other nutrients of the germ is not accounted for. The fine flour of our ancestors was not impoverished to the extent of modern white flours. Stone-milling ground the wheat germ and much of the bran so finely that they could not be separated out effectively by bolting. Modern roller-milling operations do not grind the wheat germ but flatten it so that it can be bolted out of the fine flour.

In the degumming process of vegetable oils, all the phosphatides are lost. Only a very small proportion of

the precipitated phosphatides is added to food again. Though minor sources of phospholipids and phytin remain in some vegetable foods (legumes), the equilibrium cholesterol/phospholipids in the average diet is artificially shifted in favour of cholesterol. In the manufacture of animal edible fat the phopholipids are separated from the fatty tissue by passage of live steam, churning or rendering, but cholesterol remains with the fatty phase. Eastern peoples rely much more on non-fractionated cereals for carbohydrate supply and oil-containing seeds or crude oils instead of degummed and hydrogenated refinery products for fat supply.

Let us try to follow, qualitatively, what is done to oilseeds in the manufacture of shortening and margarine. Soybeans are the main source of fat of the Chinese and (together with cotton seed) the main source of shortening and margarine of the American people. The soybean is an almost complete food on which, supplemented with small amounts of cereals and vegetables, entire populations have greatly depended for very long times. Soybean flour is a valuable source of high quality proteins and essential fatty acids. It exceeds egg yolk in phosphorus content and is the richest source of vegetable phosphatides and one of the richest sources of thiamine, riboflavin, pantothenic acid, magnesium and manganese. It has moderate pro-vitamin A value. On its way through extraction, refining and bleaching, it loses all of these nutrients, except the oil. Hydrogenation destroys the essential fatty acids. The addition of powerful synthetic antioxidants is allowed in many industrialized countries, adding another factor in the deactivation of fat towards oxygen.

HYDROGENATION OF ESSENTIAL FATTY ACIDS

Hydrogenation changes the oils in such a way that the resulting product is principally different from any natural fat. Hydrogenation does not attack the unsaturated fatty acid at random, but shows preference for linoleic acid. The rate at which hydrogen reacts with linoleic acid may be as much as 50 times as high as its rate of reaction with oleic acid. The newly synthesized fatty acid is an isomer of oleic acid, not occurring in nature. There is no natural fat without linoleic acid, but fats, poor in linoleic acid are rich in short chain saturated fatty acids. From the composition of more than 50 commercial fats we have found but one exception to this rule (Cocoa butter). We give only a few examples:

Percentage by weight

	sat. acids C_4-C_{14}	linoleic acid	Important source of fat in:
Olive oil	1	15	Mediterranean area
Peanut oil	0.5	26	Africa, India, China
Cottonseed oil	1	48	United States
Soybean oil	0.5	52	U. S., China
Coconut oil	80	2	Philippines, Indonesia
Lard	2	6-14	Western countries
Butter	25	2-4	Western countries
Cocoa butter	0	2	———
Palm kernel oil	70	0.5	Africa, Indonesia
Palm oil	2.5	10	Africa, Indonesia

Hydrogenation disturbs this naturally existing equilibrium. The fat of Eastern, Mediterranean and South American peoples is of the short chain type or of the essential fatty acid type. All natural phospholipids belong to the essential fatty acid type. C_4-C_{14} acids have not yet been identified in phospholipids, whereas linoleic acid always forms a very substantial percentage and arachidonic acid, seldom or never encountered in triglycerides, is abundant in some phosphatides, for instance in brain.

BUTTER

The diet of Asian and African peoples includes little or no butter. In Western Europe butter is greatly superseded by margarine, but it amounts to about half the fat consumption of the American people. Butter, by its peculiar composition, takes a position, difficult to evaluate. Milk contains both phospholipids and cholesterol. Usually, phospholipids follow fat in the manufacturing process of dairy products. However, in the churning of butter a substantial portion of the phospholipids goes into the butter milk, whereas practically all the cholesterol moves into the butter (250 mg.% in Dutch dairy butter). The fatty acids of butter include 25% of C_4-C_{14} acids and 2-4% of linoleic acid.

ATHEROMATOSIS AND COMPLEX LIPIDS

Most students of atherosclerosis have been led to the view that the circulating blood lipids are importantly related to atheromatosis. Serum lipids are at least partly combined with proteins. However, combination of cholesterol, cholesterol esters or triglycerides with proteins has never been shown and is not very likely from a chemical point of view. Contrast this with the zwitterion structure of the nitrogenous phosphatides where ample opportunity is present for the attachment of amphoteric amino acids. Genuine hydrophylic protein-phospholipid complexes have been isolated from eggs (26) and the student of phospholipid purification has always been faced with the problem of removing tenacious nitrogenous impurities. Blood serum can hold appreciable amounts of cholesterol, cholesterol esters and triglycerides in aqueous solution, but when serum lipoproteins are disrupted by a potent lecithinase, the lipids separate from the protein fraction and turbidity develops, related to total serum lipids (27). The suggested correlation between food and lipoprotein distribution on one hand and the occurrence of abnormal lipoproteins in coronary disease (28) on the other hand may very well be in line with the conception that food contains factors which enable or prevent the formation of stable lipoproteins. The capillaries of blood vessels provide a means of exchange between the blood stream and lymph (29, 30). Lipids not combined to stable lipoproteins would not be expected to pass the endothelial cells and internal elastic membrane. Neutral fats or chylomicrons are unable to penetrate the walls of excised vessels (30). Furthermore blood vessels may show considerable metabolic activity (31), on which our knowledge is still very scanty.

DISCUSSION

Cardiovascular disease is becoming a health problem, second to none in the industrialized countries. Such long term studies as made by Morris in England

TABLE I.

Parts per million

	magn.	iron	mang.	copper	phosph.	choline	inositol	thiamine	pantothenic acid
Whole wheat flour	1.600	38	46	8	3.800	900	2.500	5	8-12
White flour	300	8	8	2	1.000	500	300	0.8	4
Bran	4.500	130	70	12	12.000	1.500		7.5	25
Germ		86		13	10.000	4.000	7.700	35	30
Rice (brown)	1.200	55		4	3.000			3	
Rice (polished)	280	9	10	2	1.000	900		0.4	
Rolled oats	1.400	40	50	7	3.600	1.500		8	
Peanuts	1.700	19			3.900	1.600	1.800	3-6	25
Soybean flour	2.300	30	40		5.800	3.500		9-12	18
Beans (dried)	1.600	100	15	9	4.600		3.300	5-6	
Peas (dried)	1.400	60	20	8	4.000	3.000	3.000	5-9	30
Eggs (fresh)	130	30	0.3	3	2.300	4.000	330	1-1.5	20
Liver (fresh)	220	120	4	35	3.800	5.000-7.000	500	3-4	40-75
Meat	200	25			1.800	900	100	1.5	10
Fresh milk	120	2			900	150	180	0.4	1-4
Cheese	420	10			6.000	500-800	250	0.5	10
Potatoes	270	7	1.5	1.5	560		300	1-1.5	2-6

(32) provide evidence that coronary thrombosis and myocardial infarction were rare before the first world war and have since become common and that as a common disease they are new and not merely newly recognized. Coronary disease is not a problem of old age but may be considerably advanced in adolescence (33, 34), long before any clinical symptom appears.

Abnormal lipid precipitation is due to a complicated metabolic disturbance, at least partly dependent on nutrition. In this article the attention is focused to nutritional imbalance as a possible extrinsic factor. Modern production methods increasingly stabilize wheat flour and fats against decay by enzymes and atmospheric oxygen. An adjoint list of nutrients gives an impression on some losses in industrial processing.

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ABSTRACTS ON NUTRITION

SUKIENNIK, S.: *Periods of remission in diabetic patients.* Dapim Refuiim, 14, 1, Feb. 1955, 11.

Four patients, one adult and three adolescents, in whom rather long periods of "remission" of diabetes occurred are presented. They began as severe diabetics who responded promptly to diet and insulin. After a short period of treatment it was found that insulin could be withdrawn, although continued diet was advised. One patient who was placed on a normal diet suffered a sharp recrudescence of the disease. When the period of remission ended, there was noted an aggravation of the diabetes, and they all showed signs of grave, intractable diabetes. The author feels that all severe diabetes should be continued on diet and insulin and no allowances made for remissions, and certainly, in any case, the diet should be rigorously followed.

MAGID, G. J. AND STEENROD, W. J.: *Intravenous fructose in the management of diabetic emergencies.* Bull. Mason Clin., 9, 1, March 1955, 10.

Inasmuch as fructose enters into the metabolism and is stored in the liver as glycogen without the help of insulin, fructose appears to be a valuable adjunct particularly in the management of diabetic acidosis and in the cases of patients with diabetes undergoing surgical operations. Thus far the results have been promising.

ROSE, C. AND BARRON, J.: *Anaphylactic shock as a complication of insulin coma therapy.* Brit. Med. J. Mar. 5, 1955, 583.

Insulin coma therapy was used on a paranoid schizophrenic patient. From Oct. 22 to Oct. 31, he received daily treatments. November 1 was a rest day. On Nov. 2, an intravenous injection of 160 units of soluble insulin was given. Within 5 minutes coughing and retching occurred suggesting anaphylaxis. Intravenous adrenalin was used and general treatment for shock was begun. Bronchospasm and vasomotor collapse remained very pronounced so that intravenous 33½% dextrose and nikethamid were given. Even by Nov. 4, in spite of anti-allergic treatment, he remained rambling and confused, although mentally accessible. By Nov. 14, no significant mental change resulting from the anaphylaxis could be noted. Intradermal tests of sensitivity to all forms of insulin remained positive even until April. Passive transfer reactions also were positive. These features distinguish true anaphylaxis from the anaphylactoid reactions. The patient was not sensitive to various meat extracts nor to the preservatives used in the insulin. It is thought that the anaphylaxis was due to some impurities in the insulin. Benefit was obtained from the use of anti-allergic drugs.

CLEMENTS, F. W.: *The teeth and food.* Med. J. Australia, Feb. 26, 1955, 297.

Clements shows, briefly, that good nutrition in the broadest sense is essential to good teeth and, furthermore, that dental caries increases with the use of sugar and carbohydrate foods. He further points out that it is practically impossible to limit sugary foods in children because the parents themselves over-indulge. Consequently the control of caries becomes a sociological problem in which there is need to elevate the ideal of non-carious teeth as a mark for all to aim at and in

which education regarding proper diet forms an essential part. Fluoridation of drinking water is a practice for which there are increasing public demands.

ISKRANT, A. P. AND KURLANDER, A. B.: *Diabetes mellitus mortality in the continental United States, 1950.* Jour. Chronic Dis., 1, 4, April 1955, 368.

In 1950 diabetes caused 24,000 deaths, or a mortality rate of 16.2 per 100,000 of population. The death rate is highest in white females, followed by non-white females and white males. It increases with age in all groups and is higher in non-whites in the early years of life but higher in whites from about age 65 on. Mortality is considerably higher in married women than in men or single women in the older age groups in which the disease mortality is most significant. The rate in married men also is somewhat higher than in single men in these ages. Death from diabetes is reported at higher rates from cities than from rural areas. The Northeast and North Central states have the highest death rates and the South and West the lowest. Crude death rates from the disease have risen since 1900 with a tendency to level off in recent years. Since 1920, death rates for those under 45 (particularly those under 15) have decreased considerably.

DEB, A. K.: *Modified insulin and vitamin B-complex treatment of some common mental ailments.* Calcutta Med. J., 51, 11, Nov. 1954, 375.

Deb treated 3 cases of schizophrenia, 1 case of hysteria with some psychotic symptoms, and 1 case of anxiety neurosis by insulin injections along with injections of a vitamin B complex preparation. The dose of insulin given once daily or less frequently varied from 10 units to 140 units. Hypoglycemia was controlled by a drink of sugar in water following the injection of insulin, occasionally by glucose I.V. Excitement and nervousness were controlled by Rauwolfia powder and/or other sedatives. The striking result was marked improvement in the mental condition of all these patients. Possibly the treatment assisted the brain cells better to utilize carbohydrate. Deb admits he cannot explain the good results.

HEARNE, R. B.: *Coma and hyperglycemia following islet-cell tumor removal.* Northwest Med., 54, 111, Mar. 1955, 260.

A Japanese male, aged 64, suffering from hyperinsulinism and operation revealed an islet-cell tumor 1.5 cm. in diameter which was removed with the tail of the pancreas and the spleen. It proved to be an insuloma, with some suspicion of malignancy. He eventually made a complete recovery. However, 24 hours after operation he entered a shock-like condition with thready pulse of 130, and a blood sugar of about 500 mg. percent. The injection of insulin brought him out of this serious condition within ten minutes. His preoperative blood sugar readings had been from 11 to 17 mg. per cent. It appeared that he could not tolerate the elevated blood sugar. There was no evidence of diabetic coma, no acetone in the urine, and cerebral and cardiovascular lesions could be ruled out. Any explanation of this peculiar phenomenon of a high blood sugar associated with shock and stupor, suddenly relieved by insulin, cannot be given in the light of our present knowledge of physiology.

RUCKS, W. W., JR.: *The reversibility of the central nervous system manifestations of prolonged hypoglycemia: report of a case.* Amer. Pract. & Dig. Treat., 6, 3, March 1955, 406.

Rucks describes the case of a woman of 60 subject to spells of confusion and peculiar behavior, with frequent morning episodes of mental incapacity before breakfast which were helped by giving grape juice. For several years the case went begging a diagnosis. In a sanitarium where she had received shock treatments, a low blood sugar had been casually noted. Finally she was admitted to a hospital, having been in coma for six hours. A diagnosis of active islet-cell tumor of the pancreas was made, operation performed and an insuloma 1.5 cms. in diameter was removed from the center of the body of the pancreas. Following the operation she developed high blood sugar requiring insulin for a time. Her mental condition did not reverse itself at once, but ultimately she returned to a normal mental state. The case seems to illustrate the fact that whereas, in some persons, even one serious attack of hypoglycemia (as, for example, following too large a dose of insulin) may cause irreparable and permanent brain damage, there are other persons who have the power, under favorable circumstances, to emerge from prolonged and repeated attacks of hypoglycemia without obvious cerebral injury.

COLES, B. L. AND JAMES, U.: *Use of cobalt and iron in the treatment and prevention of anemia of prematurity.* Journal-Lancet, Mar. 1955, 79.

The study included 126 infants who were divided into four groups. Of these, 83 were followed for six months or longer. Group 1 acted as controls. Group 2 received 10 g. cobalt sulfate daily from one to twelve days. Group 3 received 20 mg. cobalt sulfate daily from four to eight weeks. Group 4 received 20 mg. cobalt sulfate and 4.5 gr. ferrous sulfate daily from four to eight weeks. Cobalt appears to be of value in the prevention of early anemia in premature infants and, if iron is given simultaneously, the risk of an iron deficiency anemia developing after the fourth month is considerably reduced. Cobalt has no toxic effects and no unfavorable influence on the weight gain in the dosage employed. The mode of action is uncertain but two possibilities appear—(1) a direct action on the erythropoietic tissues in the bone marrow; (2) a possible catalytic action enabling iron to be more readily utilized for hemoglobin synthesis.

IWATSURU, R., KATO, I. AND KANAGAWA, Y.: *The mechanism of anemia induced by K.I.K. reaction.* Wakayama Med. Reports, 2, 1, May 1954, 1.

In 1937 Iwatsura found that the gastric juice of persons with cancer of the stomach, when injected into rabbits, produced a marked anemia. This test (K.I.K. reaction) was found to be diagnostically reliable. The present authors now show that this is not a true anemia but rather an oligocythemia caused by retention of red blood cells in endothelial tissues, especially spleen and liver. It is thus an anemia of "distribution."

HARADA, M. AND HORIGUCHI, G.: *Bone and nutrition: experimental studies on changes of bone and bone marrow in hypoproteinemia.* Wakayama Med. Reports, 2, 1, May 1954, 7.

Hypoproteinemia was produced in rabbits by both of two methods—low protein diet and daily bleeding. A marked fall in serum protein levels occurred in the feeding experiments but not in those rabbits which were bled. Bleeding stimulated the bone marrow but low protein diet caused collagenous marrows. The protein-starved rabbits showed thinning of epiphyseal cartilage and trabecular atrophy. Protein metabolism appears closely related to the osteogenic mechanism.

EDITORIAL

SUBTOTAL GASTRECTOMY FOR PEPTIC ULCER

Possibly all will agree that in persons under 50 years of age suffering from peptic ulcer which does not respond to ordinary medical treatment, the operation of subtotal gastrectomy has proved to be, on the whole, a quick and ready solution to the problem. Yet the high incidence of recurring (stomal) ulcer, the limited capacity of the stomach to hold food, the "dumping" syndrome and the not uncommon interference with general nutrition due to faulty absorption of vitamins, iron, fats and proteins, give rise to the serious question as to whether or not this mutilating operation actually is justifiable. In women, particularly, severe iron-deficiency anemia is prone to develop, requiring continued treatment. Neither has sufficient emphasis been placed upon the rather high incidence of pulmonary tuberculosis following the operation. This point was recently emphasized by Anderson, Gunn and Watt (1) who, following a series of 481 partial gastrectomies, found 16 persons developing tuberculosis, half of whom succumbed to the disease.

It is the internist, in particular, who ordinarily has to deal with the unfavorable after-effects of the operation and many internists have become seriously impressed with the apparent fact that this operation not only frequently fails to cure the ulcer tendency, but often gives rise to the unfortunate effects just mentioned. There may eventually be a partial return to the less mutilating operation of gastro-jejunostomy with (or without) vagotomy.

The ungarnished truth is that as yet no cure for peptic ulcer really exists. Some cases respond well to medical regimes but tend to recur. We have a feeling that certain emotional characteristics of the ulcer people actually represent the fundamental stumbling block to the success of any form of treatment. It is not easy to alter human personality or rearrange the standard of values or the emotional reactions to ordinary events and interpersonal relationships. We suspect, however, that some form of psychotherapy will ultimately be found which may so change the individuals, even to the depths of their personalities, that the ulcer tendency may be permanently removed.

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BOOK REVIEWS

DIFFERENTIAL DIAGNOSIS OF INTERNAL DISEASES: CLINICAL ANALYSIS AND SYNTHESIS OF SYMPTOMS AND SIGNS ON PATHOLOGICAL BASIS. Julius Bauer, M. D., F.A.C.P., Grune and Stratton, New York. 1955. $15.00.

There is no question that Bauer has written an interesting and useful book. The approach to differential diagnosis is by (a) Leading symptoms and (2) Leading signs. In both sections of the book a given symptom or sign is analyzed with respect to the over-all clinical picture. The volume will serve the purpose of reminding the practicing physician of many things he has probably forgotten. It will serve as a valuable hand-book for current study when any group of signs or symptoms is met clinically that does not at once make sense. It would be difficult to see how a better treatise could have been written on diagnosis in 1,000 pages. Naturally, this is not a systematic practice of medicine and treatment has had to be omitted.

THE CARE OF YOUR SKIN. Herbert Lawrence, M. D., Little, Brown and Company, Boston, May 1955, $2.50.

This is a special book, written for the laity, and dealing with the treatment of acne. A perusal of the volume suggests that it would be a safe and satisfactory one to hand to a patient suffering from this disturbing disease. Doctors desiring to have a supply may obtain the same at bookseller's discounts from the publishers.

MEDICAL PROGRESS. (A REVIEW OF MEDICAL ADVANCES DURING 1954). Morris Fishbein, M.D., Blakiston Division, McGraw-Hill Book Co., Inc., New York 1955, $5.00.

The present is the third in a series of annual volumes of unusual value, because only what is regarded as *actual progress* is given space. In this way, these books

are by no means "year books" in the ordinary sense. In the present volume considerable space is devoted to new drugs. As Fishbein states in his preface, medicine is becoming more and more chemical, so that older physicians may have some difficulty following the text with ease. The section on gastroenterology is well written by David J. Sandweiss and Frank P. Brooks. For the busy physician, desirous of keeping up to the minute, this book will perhaps serve his purpose better than any other we know of.

LES GASTRITES. F. Moutier and A. Cornet. Masson et Cie, 120 Blvd. Saint-Germain, Paris 6, 4400 francs.

This is the first exhaustive volume in French medical literature devoted to the various forms of gastritis and represents many years of observation and research. Atrophic and hypertrophic gastritis are recognized as separate and valid entities and the nature of their pathogenesis and evolution is traced, as well as their relationship to peptic ulcer and gastric and duodenal hemorrhage. The book is profusely illustrated and it should take its place as one of the truly valuable contributions to gastro-enterology.

ION EXCHANGE AND ADSORPTION AGENTS IN MEDICINE. Gustav J. Martin, Sc.D. Little, Brown and Co., Boston. 1955. $7.50.

Martin has worked for over a decade on ion exchange resins, and in his new book, which summarizes our knowledge on the subject, as well as on adsorption phenomona, he emphasizes the ideal of prophylaxis as opposed to treatment. Anion exchange agents in peptic ulcer and for sodium reduction have become familiar to all physicians. Martin holds that in the etiology of all degenerative diseases, the absorption from the intestine of small quantities of toxic chemicals represents an important element. While this may appear to be a return to the theories of Metchnikoff,—theories which were generally abandoned during the past 30 years,—nevertheless, Martin's presentation of the subject contains certain persuasive facts and arguments. The book is of value to those who are interested in all possible angles in the study of the pathogenesis of human ills.

GENERAL ABSTRACTS

BISHOP, J. F.: *Mild ulcerative colitis.* Am. J. Gastroenterology, 23, 1, Jan. 1955.

From a study of 40 cases of ulcerative colitis of his own and 10 cases "borrowed" from an internist friend, Bishop emphasizes that the majority of cases in which the diagnosis of ulcerative colitis can be made are more or less mild, abortive or mild-recurring. Only 4 of the 50 cases reviewed required surgery. Bishop seems to think that there is some kind of connection between mucous colitis and ulcerative colitis. He found that months or even years of nervous diarrhea or constipation preceded the onset of bleeding in many cases of ulcerative colitis. Half of his cases did well with no treatment except reassurance, antispasmodics and mild sedation. In 35 percent, Nisulfazol (an insoluble sulfamide) was used with good results. In 5 cases ACTH was used because of poor response to other measures. Bishop cannot see any sense in using a low-roughage diet, as it may lead to dietary invalidism. A high protein intake is mandatory. Vitamins are given empirically.

ROSE, T. F.: *The inflamed appendix abnormally situated in the abdominal cavity.* Med. J. Australia, Jan. 22, 1955, 102.

In 1050 appendectomies, there occurred 12 instances in which there was an abnormal situation of the inflamed appendix in the abdominal cavity. In 8, the abnormality was due to the cecum being out of place,—transposition, malrotation, non-descent. In 4 cases the appendix itself was abnormally long. Such cases may cause great difficulty in diagnosis because of the position of the appendix but little harm will ensue if it is remembered that abdominal pain of ever-increasing intensity is a surgical emergency.

MITCHELL, R. G.: *Intussusception of vermiform appendix in allergic children.* Brit. Med. J., Jan. 29, 1955, 265.

Two cases are described, one in a boy of 3 and the other a girl of 16 months, in which the appendix intussuscepted into the cecum and ascending colon. In the boy, a large mass was palpable in the right side of the abdomen. In the girl, x-ray barium studies showed a filling defect of the cecum. Both were cured by surgery. Both children had strong histories of allergy and this fact complicated the diagnosis.

JOSKE, R. A. AND FINCKH, E. S.: *Hepatic changes in human brucellosis.* Med. J. Australia, Feb. 19, 1955, 266.

The hepatic changes in 20 cases of proven brucellosis at the Clinical Research Unit of the Royal Melbourne Hospital are reviewed. In 12 cases there were symptoms and signs related to the alimentary tract. These included abdominal tenderness, enlargement of the liver and spleen, jaundice and diarrhea. Abnormal liver function tests were not infrequent. Twelve of the 13 liver biopsy specimens obtained from 10 patients showed abnormalities, including small lymphocyte collections, specific epithelioid cell granulomata, portal tract infiltration and fibrosis, hemosiderosis and fatty change. One patient with chronic brucellosis and cirrhosis came to autopsy, having died from massive hemorrhage from esophageal varices. It is probable that this cirrhosis was a form of chronic brucella hepatitis, and that other cases studied represented less advanced forms of hepatic brucellosis.

KHAN, S. U.: *Management of malignant stricture of the esophagus.* J. Pakistan Med. Assn., 4, 4, Dec. 1954, 137.

In inoperable cancer of the middle third of the

esophagus, Khan uses Souttar's tube provided x-ray studies show that the growth has not involved more than 7 cms. of the gullet. First a fine Jackson bougie is passed to dilate the stricture, the tube inserted and an x-ray taken to make sure it is in the proper position. The diet must be liquid or semi-liquid. Eventually the tube becomes blocked by the growth. Occasionally it slips down and is passed per rectum. In 12 cases, no perforation was caused by the use of the tubes. Where the tube cannot longer be used, a permanent gastrostomy is done for feeding purposes.

KIRSH, I. E.: *Benign and malignant gastric ulcers: roentgen differentiation: an analysis of 142 cases proved histologically.* Radiology, 64, 3, March 1955, 357.

An analysis was made of the roentgen diagnosis in 142 histologically proved gastric ulcerative lesions, 120 benign and 22 malignant. The incidence of certain radiographic criteria in the 2 groups was compared. Mucosal folds which radiate from the edge of the crater were found in 42 percent of the benign ulcers and in none of the malignant ulcers. Abnormal folds and a filling defect in the region of the ulcer were found in 19 of the 22 malignant ulcers and in only 14 percent of the benign ulcers. Little difference was noted in the 2 groups in the following occurrences,—penetration beyond the gastric lumen, undermining of the border of the crater, irregular ulcer base, and duodenal deformity. Of no differential value were the location of the ulcer, size of the crater, rate of healing or the presence of a normal incisura.

JOHNSON, A. S.: *Small bowel obstruction by a vegetable bezoar.* Harper Hosp. Bull., 13, 1, Jan.-Feb. 1955, 43.

A colored woman with hypertension complained of recurring mid-abdominal cramp and vomiting. Enemas were ineffectual. X-ray films showed obstruction of the jejunum. Operation revealed a rather large bezoar in the mid-jejunum causing obstruction, composed of vegetable matter. She had eaten a large serving of turnip greens 5 hours before the onset of symptoms. The bezoar was easily removed and she made an excellent recovery.

JONES, R. F.: *Gastric ulcer: an organized plan of management.* Bull. Mason Clin., 9, 1, March 1955, 32.

All patients with gastric ulcer are studied intensively, clinically, by x-ray and by gastroscopy. Medical treatment is not used if the x-ray appearances make one suspect cancer (no lesion wider than 2.5 cm. should be medically treated if the ulcer is on the greater curvature, if achlorhydria after histamine stimulation persists, if the ulcers are bleeding, penetrating or obstructing, if the ulcer is prepyloric or on the posterior wall where gastroscopy is useless, or if the patient cannot be adequately observed for several weeks). Medical treatment includes 10 days' rest in hospital with strict diet, antacids, sedatives and anticholinergic drugs. During this 10 days symptoms should disappear, and then further x-rays are made. If the ulcer has become larger, medical treatment is discontinued. If healed or healing, the patient is x-rayed again in 3 weeks, at which time a large percentage of benign ulcers will be healed. However, re-x-ray is done about every 3 weeks till certainty exists that the lesion is healed.

LIEBERTHAL, M. M.: *Irritable colon syndrome.* Connecticut Med. J., 19, 2, Feb. 1955, 86.

The author used the accepted dietary, psycho-therapeutic and pharmacological methods of treating a group of cases of irritable colon. Least improvement was found in those who were least amenable to psychotherapy. Recovery, in cases in which it did occur, was hastened by using Konsyl (a hydrophilic colloid derived from blond psyllium seed). Some cases, however, were resistant to improved elimination even with this assistance.

MUSGROVE, J. E.: *Posterior penetrating gastric ulcer.* Canadian Med. Assn. Jour., 22, 5, Mar. 1, 1955, 342.

A posterior-wall gastric ulcer with penetration into the pancreas is almost invariably benign. With x-ray studies plus operative palpation and inspection, the surgeon should be able to rule out malignancy in almost 100 percent of cases. Understanding of gastric pathology is extremely important for it means the difference between conservative and radical surgery, with the concomitant difference in operative mortality and postoperative morbidity. The author describes a method of doing a partial gastric resection which conserves as much stomach as possible and allows the Billroth I type of gastrointestinal union to be performed. Four case reports are given. One case illustrates how radical the surgery may be in a mistaken diagnosis of cancer. It is best to err on the side of conservatism, for if a lesion ultimately is proved malignant, a good palliative operation has been done. In about 95 percent of cases, the lesion will prove to be benign.

STONE, C. S.: *Technical considerations in surgery for acute cholecystitis.* Bull. Mason Clin., 9, 1, March 1955, 24.

The gallbladder should be removed in acute cholecystitis when possible without injury to the common duct or blood vessels. When cholecystectomy is not considered safe to perform, cholecystostomy should be done. In the majority of cases, however, the organ may be safely removed.

WASS, S. H.: *Chronic pain in the right iliac fossa.* Brit. Med. J., Mar. 26, 1955, 752.

The author enumerates and briefly describes the many organic conditions which may cause pain in the right iliac fossa, including spastic colon, ureteritis, stone in the ureter, spinal arthritis, and finally that much maligned condition, chronic appendicitis. Where there is chronic tenderness at McBurney's point, with either recurring subacute inflammatory attacks, or with appendicular colic, the diagnosis appears to be justified and the appendix should be removed. The results often are good. In fact, the removal of an apparently normal appendix frequently causes a cessation of the tenderness or pain. Wass mentions the group of psychoneurotics who, because of distress in the right iliac fossa, without any evidence of organic disease, desire operation. He feels it is better, in these cases, to re-

fuse operation rather than to do an operation which will become merely the first of a long series of unnecessary laparotomies.

CANCELMO, J. J.: *Stellate fissuring in gallstones.* Radiology, 64, 3, March 1955, 420.

Three cases are presented in which fissuring of gallstones was found. This phenomenon often serves as the sole basis for a diagnosis of cholelithiasis. The fissures may be recognized in the x-ray films as stellate areas of radiolucency. In one of the cases, the stones were found to contain gas.

HIGHTON, T. C.: *A clinical trial of a derivative of a bile salt in the treatment of rheumatoid arthritis.* New Zealand Med. J., 53, 298, Dec. 1954, 569.

Data are presented on a total of 56 patients who were treated by bi-weekly injections of 200 mg. of sodium tri-ketocholanic acid. Of these 64.3 percent derived benefit. The injections have to be continued for at least 2 years. The results obtained are better than those obtained by steroid therapy and better than occurs in the natural history of the disease. The mode of action of this therapeutic agent is now under investigation.

BURT, L. I. AND MASEL, H.: *Cholecystitis glandularis proliferans (diverticula of the gall bladder).* Med. J. Australia, Feb. 19, 1955, 270.

Three cases are described which would come into the category of diverticula of the gall bladder (or cholecystitis glandularis proliferans). Various names, such as diverticula, or diverticulosis, cholecystitis granularis proliferans (cystica), Rokitansky-Aschoff sinuses, Luschka's cysts and chronic cholecystitis cystica have been used to describe varying degrees of the same pathological condition. A satisfactory solution to this impasse in nomenclature is very difficult, as the term diverticulosis suggests absence of inflammation, while the term cholecystitis glandularis stresses the presence of inflammation. While theories as to etiology differ, it would be better to rely on the two alternative names used in the title of the article. With the advent of higher iodine content in the cholecystographic media, more of these structures should be visualized by cholecystography.

ANDERSON, C. D., GUNN, R. T. S. AND WATT, J. K.: *Results of partial gastrectomy in the treatment of peptic ulcer.* Brit. Med. J., Feb. 26, 1955, 508.

A study of 481 cases in whom partial gastrectomy was performed for peptic ulcer, convinces the authors that only about 4 percent of patients are dissatisfied with the results. However, a large number (29.4%) are troubled by mild or severe post-gastrectomy symptoms, although these symptoms are more easily tolerated than the pain of ulcer. The rate of recurrent ulceration is high. There is a tendency to anemia, more so in females, and possibly gastroenterostomy should be done in women. In either sex at ages over 50, gastroenterostomy is to be preferred. Even in patients who do well following gastrectomy, nutrition remains substandard due to faulty absorption or iron, vitamins, fat and protein. This nutritional fault almost certainly explains the rather high incidence of pulmonary tuberculosis in these cases. In the present series 8 died of the disease and 8 others contracted it but are still living.

FRENCH, W. E.: *The surgical aspects of biliary disease.* Jour. Arkansas Med. Soc., 51, 10, March 1955, 222.

French thinks that silent gall stones should be removed to prevent future trouble. He believes that cholecystography has become a reliable means of studying the function of the gallbladder. In cholecystectomy, no structure should be ligated until the cystic duct, cystic artery and common duct are clearly visualized. Most injuries to the common duct are preventable.

CONNELLY, M. E. AND MAYO, C. W.: *Late recurrence of regional enteritis: report of a case.* Proc. Staff Meet. Mayo Clin., 30, 4, Feb. 23, 1955, 68.

We are coming to recognize the fact that regional ileitis, following operation (no matter how well performed) does not necessarily "burn itself out." Recurrences in the first 7 years following operation have been reported. Crohn and Janowitz report a recurrence 12 years after surgery. The present authors now report the longest-delayed recurrence yet seen,—19½ years following operation.

WYNN, V. AND GARROD, O.: *Spontaneous and induced water intoxication in two cases of hypopituitarism.* Brit. Med. J., Feb. 26, 1955, 505.

An abnormality of water balance is described in two cases of anterior hypopituitarism. Although their fluid intake was not forced, they retained water in excess of electrolytes, causing dilution of the body fluids and symptoms of water intoxication. The diagnosis was suggested by gain in weight and a very low plasma sodium concentration. When cortisone was given there was a prompt water diuresis and the plasma sodium rose to normal concentration. Water retention may not be very rare in anterior hypopituitarism, although only one other case of it has been reported. Water excretion tests of adrenal function precipitated acute symptoms of water intoxication including nausea, vomiting, extreme prostration, mental confusion, and stupor. This was probably because there was already excessive dilution of body fluids, although unrecognized before the tests. Therefore a water excretion test should not be carried out until the plasma sodium concentration is known. If symptoms due to water retention occur in patients with hypoadrenal function, cortisone should be given, whereupon the excess water will be rapidly excreted.

HONIG, E. M.: *Psychosis and peptic ulcer.* Bull. Menninger Clin., 19, 2, Mar. 1955, 61.

Several groups of statistics have been presented by various authors, seeming to indicate that peptic ulcer is much less common among psychotics than in the general population. The ratio appears, from these reports, to be from 1:3 to 1:100. Honig points out that it is seldom easy to diagnose ulcer in psychotics, since those who are least communicative may even harbor a perforated ulcer without any complaint of any kind. In a special study of 22 cases in which the dual diagnosis of psychosis and ulcer was made, Honig found that in the majority (68%) the two diseases were simultane-

ously active. In 14% of the cases, there was an alternation between the two diseases, such that the psychosis subsided with the onset of the ulcer. In 18% no temporal relationship could be ascertained. Honig found ulcer affected schizophrenics much more frequently than manic-depressives. Certainly it is true that peptic ulcer and a regressive psychosis are not incompatible. In 15 cases of coexistence of psychosis and peptic ulcer, 2 patients had undergone a bilateral prefrontal lobotomy. These two cases developed ulcer after their operation.

SCHLITZ, F. H.: *Phases of pancreatic disease with presentation of case reports.* J. Pakistan Med. Assn., 4, 4, Dec. 1954, 125.

The following laboratory procedures are of value in diagnosing pancreatic disease,—study of enzyme levels in the blood, urine and peritoneal fluid; starch and glucose tolerance tests; studies of duodenal contents and the stools; blood coagulation factors; study of the x-ray pictures. The morbidity and mortality of acute pancreatitis have been greatly reduced by conservative treatment. Partial and total pancreatectomies are feasible procedures especially when early diagnosis has been made.

MASSIK, P. *and* Wheatley, F. E., JR.: *The recognition of air in diverticula of the colon as a diagnostic aid.* Radiology, 64, 3, March 1955, 417.

During a nine-month period in which 370 barium enemas were done, air in colonic diverticula was recognized on the A-P scout film of the abdomen in 12 cases. Scout films may thus furnish valuable aid in arriving at a diagnosis.

ASHBY, D. W. AND WHITEHOUSE, D.: *Treatment of hemorrhages from peptic ulcer by continuous intragastric milk drip.* Brit. Med. J., Feb. 26, 1955, 512.

Of 153 ulcer patients admitted to hospital as emergency cases for hematemesis or melena, 100 were treated by continuous intragastric milk drip given from the time of admission, while 53 were treated as a control group by hourly milk feeding and early generous increase of food intake. Both groups received adequate blood transfusions. The milk drip method did not obviate the necessity for surgery after continued bleeding in old people, nor has it, thus far, produced a fall in mortality of this group. The drip method tended to diminish the duration of bleeding, and more than 2 recurrent bleedings in hospital were very uncommon in this group, but the number of recurrences did not differ much in the two groups. The drip-treated group showed earlier reassurance, confidence and freedom from shock than the control.

SOUTHWICK, H. W., SLAUGHTER, D. P. AND BOLLINGER, J. A.: *Idiopathic hypertrophic pyloric stenosis in an elderly adult.* Illinois Med. J., 107, 3, March 1955, 139.

A woman of 82 presented symptoms and x-ray findings consistent with a diagnosis of hypertrophic pyloric stenosis. After blood transfusion she was subjected to a partial gastric resection with a Billroth I reconstruction. She made an uneventful recovery. The specimen showed hypertrophic stenosis of the pylorus but no evidence of ulceration or cancer. It is believed that the lesion represents a persistence of the infantile congenital lesion in which there are few symptoms till later in life. The case also illustrates the truth of Stewart's dictum, "too old not to be operated on."

ROSS, W. D., FINBY, N., AND EVANS, J. A.: *Intramural diverticulosis of the gallbladder (Rokitansky-Aschoff sinuses).* Radiology, 64, 3, Mar. 1955, 366.

Two new cases with radiological demonstration of intramural diverticula of the gallbladder are presented. Eleven cases were found on review of the literature. Intramural diverticula of the gallbladder are associated with inflammatory disease and gall stones. The radiographic demonstration is an indication for cholecystectomy. All cases had symptoms suggestive of cholecystitis.

DOUBILET, H., POPPEL, M. H. AND MULHOLLAND, J. H.: *Pancreatography.* Radiology, 64, 3, March 1955, 325.

The authors describe a method of visualizing the pancreatic ducts. At operation a catheter is inserted in the duct of Wirsung and a radio-opaque fluid is injected. In cases where inflammation of the pancreas exists, the entire pancreas may be opacified. Over 200 observations were made on 100 different patients. The method appears to have real diagnostic value.

TEXTER, E. C., WHEELOCK, M. C. AND BARBORKA, C. J.: *Some problems in the diagnosis and management of regional ileitis, enterocolitis and idiopathic ulcerative colitis.* Am. Pract. and Dig. Treat., 6, 2, Feb. 1955, 216.

In a rather pessimistic description of 3 diseases named in the title, it is pointed out that while clinical differentiation may, at times, be difficult, the pathological findings are distinctive in each. The authors do not think lasting results can be obtained from medical treatment, so that they favor surgical treatment in serious cases. Steroid therapy does no lasting good. Formal psychotherapy is uncalled for in ulcerative colitis, although friendly counselling is of value.

SMITH, L. S. AND GAST, J. H.: *New aspects of old liver function tests.* Texas State J. Med., 51, 2, Feb. 1955, 67.

After a review of the value and applicability of various hepatic function tests, the authors make the following suggestions,—(1) The icterus index should be replaced by the total bilirubin determination, (2) The van den Bergh test should be discontinued as it is misleading in differentiating extrahepatic and intrahepatic icterus, (3) The bromsulphalein test should be employed with a large dose and a short time interval, (4) The cephalin-cholesterol flocculation determination can never be "stat.", (5) Prothrombic activity should be reported in percentage, not in seconds. Vitamin K_1 should replace vitamin K preparations, (6) The term a/g ratio is worthless, (7) The "normals" for albumin have been too high in the past. Globulin normals have been too low.

ANTI-SMOKING THEORIES NOT BASED ON COMPLETE SCIENTIFIC KNOWLEDGE

Atlantic City, N.J.—Claims that smoking causes "this thing or that" are generally not based on complete and accurate scientific knowledge, Dr. Robert C. Hockett, associate scientific director of the Tobacco Industry Research Committee said today.

"It has been known for generations that smoking slightly increases the pulse rate to give a lift that many persons find helpful in meeting the demands of intense modern living," he told the annual meeting of the American College of Angiology. "But beyond this, little is established scientifically about tobacco effects on the heart."

"Tobacco use has been both applauded and condemned for centuries without much being known about it," Dr. Hockett said. "It has been called a source of relaxation and enjoyment to mankind and even has been reported as killing various harmful bacteria.

"It also has been charged with leading to insanity, indigestion, sterility, impotence, baldness, and a host of other ailments. It is time that careful scientific investigation should replace folklore and tradition in such matters.

"The Tobacco Industry Research Committee is supporting scientific investigation into many phases of tobacco use and human health in order to get the facts," Dr. Hockett said. "We are not attempting to prove or disprove any particular charge, but wish only to gain sound scientific knowledge."

He said considerable research is currently being sponsored into such subjects as: the effects of tobacco smoking on the heart and blood vessels of living volunteers; the influence of smoking on the blood flow of the skin and of the muscles of the body extremities; and the measurement of coronary blood flow in humans before and after the intravenous injection of nicotine, and after smoking cigarettes.

He said the Committee has so far approved nearly a half-million dollars in research grants recommended by its Scientific Advisory Board, a group of nine noted doctors and scientists. He said grants are being made to independent scientists at leading hospitals and laboratories throughout the country.

Dr. Hockett said a primary objective of the Scientific Advisory Board, which develops and directs the research program for the Committee, is to further the search for the cause or causes of cancer, particularly lung cancer, and of cardiovascular diseases, and for the control of these diseases.

Attention also is given, he said, to research projects that will add to the understanding of tobacco smoke and its constituents, and of tobacco use by people.

Dr. Hockett said the Scientific Advisory Board operates without hindrance or influence in deciding and directing the many avenues of research. Also, he said, the scientists who receive research grants do their work in complete freedom.

"Progress will be slow and difficult," he said, "but there is every reason to expect marked advances eventually in the prevention, treatment and cure of the various constitutional diseases which are medicine's greatest present and future health challenges."

HOW MICRO-ORGANISMS HAVE BEEN TAMED TO PRODUCE LIFE-SAVING DRUGS TOLD BY McKEEN

New York, N. Y.—The manner by which micro-organisms—whose natural habitat is a bog or ditch or a pasture—have been tamed by biochemical engineers to produce such life-saving agents as antibiotics, hormones and vitamins, was described recently by John E. McKeen, president of Chas. Pfizer & Co., Inc.

Mr. McKeen, speaking here at the New York Academy of Medicine's Institute on Medical History, traced the role of industry in the mass production of antibiotics and told how the struggle to mass produce penicillin during World War II gave birth to biochemical engineering.

Biochemical engineers had the problem of mass-producing substances which are generated, along with a hodge-podge of other, unwanted substances, in micro gamma quantities, the Pfizer president said.

The end products of the biochemical engineers' work—the broad spectrum antibiotics, cortical hormones, vitamins and fine chemicals—have become realities only in the last few years, according to Mr. McKeen.

Within this short period of time, the biochemical engineer has had to master techniques of growing these micro-organisms, under controlled conditions and in commercially acceptable yields.

The biochemical engineer deals with life-cycles of organisms in which a new generation may appear every 15-20 minutes, and one organism can become 17 million in 12 hours, he told the group.

When growing these micro-organisms — particularly penicillin molds—in deep fermentation tanks, the engineer had to design equipment to maintain sterility, to control temperature and pH on a scale unheard of before in the pharmaceutical industry, Mr. McKeen said.

In the early days of penicillin production, methods used were archaic, he pointed out.

"To sterilize the volumes of material demanded by deep tank fermentation with the sterility techniques then known, would have been as foolish as trying to sterilize Lake Michigan with a Bunsen burner," according to the speaker.

He explained that to help control temperature, a modern large-scale fermentation plant swallows every 24 hours a million gallons of water. An average fermentation tank could heat a five room house.

Through these engineering feats the production of penicillin was boosted from 21 billion Oxford units in 1943 to 430 trillion units in 1954. In 1943, enough penicillin was available to treat about 28,000 patients. Last year, there was enough to treat over 570 million patients. As late as 1943, 100,000 units of penicillin cost $20 at the manufacturer's level. Today, 100,000 units of penicillin at the manufacturer's level cost less than one cent in bulk form, Mr. McKeen said.

The Pfizer president also cited the tremendous growth of the research staffs in the chemical industry during the past 20 years.

"The chemical industry today employs approximately 35,000 people in research, as opposed to 6,500 people 20 years ago. This growth has taken place for a very simple reason: research—vigorous, con-

stant, and costly research—is the lifeblood of the pharmaceutical industry," Mr. McKeen stressed.

NEW FILM CITES BENEFITS OF "POST-OP" AEROSOL USE

Chicago—A new sound motion picture film in color describing the importance of aerosol therapy following surgery was shown here for the first time to an invited audience of medical specialists.

Titled "Postoperative Aerosol Therapy," the 16-minute film was produced under the direction of Dr. Max S. Sadove, professor of surgery (anesthesiology), University of Illinois College of Medicine. Aiding in the film's direction was Dr. Reuben C. Balagot, assistant professor, Division of Anesthesiology, University of Illinois College of Medicine.

The film preview at the Palmer House, at which Dr. Sadove was host, was attended by some 100 noted anesthetists, anesthesiologists, pediatricians, surgeons and other specialists in the Chicago area, and by doctors attending the annual meeting at the Illinois State Medical Society.

The principal point made in the film is that aerosol therapy with the mucolytic detergent Alevaire is indicated in any postoperative condition in which respiratory involvement is p r e s e n t or is likely to develop. This aspect was demonstrated in the film by means of animated drawings showing normal and abnormal physiology of the respiratory tract.

Animation also illustrates how Alevaire deposits fine particles deep into the air passages, with the smallest particles reaching the lungs' air sacs. The particles thin out thick, tenacious bronchial secretions which are then eliminated by the patient, or by aspiration. In the film, the procedure is demonstrated on patients at the Research and Educational Hospital, University of Illinois, following lobectomies, tracheotomies, bowel resections and amputations.

Discussing clinical experience with Alevaire, the film states that "Alevaire has proved to be a particularly valuable and effective compound for use in aerosol therapy."

In a short talk before the film was shown, Dr. Sadove said that "medical motion pictures are a most valuable teaching aid, and every effort is being made by my associates and myself to produce films that can be used by teachers, particularly in the training of students in medical schools and post-graduate courses."

Alevaire is also used as a vehicle for administering other drugs to combat respiratory infections, the movie notes. Those cited are decongestants, vasoconstrictors, bronchodilators and some antibiotics.

Produced by Winthrop-Stearns, Inc., the film is one of a continuing series of medical motion pictures made by the company under the editorial supervision of Martin Lasersohn, M.D., vice president. Next scheduled showings of the film are at the June meetings in Atlantic City of the American Medical Association and the College of Chest Physicians.

AEROSOL THERAPY AIDS ASTHMA AND EMPHYSEMA

Boston—Continuous humidification with the "non-toxic, aerosol detergent Alevaire," combined with cold, moist air, "is most effective therapeutically" in treating such respiratory disorders as asthma and emphysema, according to a report in the *American Journal of Surgery* (89:387, 1955). Alevaire is manufactured by Winthrop-Stearns, Inc.

Drs. Maurice S. Segal and Ernst Attinger suggest that Alevaire "acts as a cleansing agent" by helping to lower the surface tension of adherent mucopurulent secretions. This condition, they add, is especially troublesome in bronchitis in small children and adults. Regarding administration, they say the aerosol should be introduced into enclosed oxygen tent units and may be continuous for one or more days, or intermittent, as needed.

"We have not observed any toxic effects from Alevaire therapy," the authors say. They recommend 100 per cent concentrations of Alevaire with alternating cold water vapor therapy, 500 cc. of each.

Respiratory infections may be caused by actual changes in the physiology of the respiratory tract. A predisposing physiological change, the doctors suggest, is hot, dry air in homes and offices that "tends to dry long tissues to some extent," paving the way for infection. There is a serious problem in managing such infections, particularly recurring bronchitis in asthmatic children and, to a lesser extent, in adults with sinobronchitic disease, asthma and emphysema.

MASSENGILL ANNOUNCES A NEW PRODUCT—NEO SEMHYTEN CAPSULES

Neo Semhyten makes possible, with a single medication, the basic control of hypertensive patients. Each ingredient is carefully proportioned to give maximum effect. Since no complicated dosage directions are needed, close cooperation of the patient is encouraged in the prescribed medical regimen as well as in faithful compliance with restrictions on activities.

Each tablet contains—Reserpine, 1 mg., Mannitol Hexanitrate, 30 mg., Theophylline, 1 Gm., Rutin, 10 mg., and Ascorbic Acid, 15 mg.

Action is not cumulative, and once the proper dosage level has been established, maintenance medication can be continued for long periods without fear of toxic reactions.

Neo Semhyten is indicated in the treatment of essential hypertension and as a prophylactic measure in combatting severe and malignant hypertension.

NURSES NEEDED

Leaders in medical, hospital, health and women's groups, alarmed by the continuing urgent need for more nurses in this country, have formed a National Committee, with headquarters in Cleveland, to support House Joint Resolution 171. This bill, introduced in the House of Representatives by Frances P. Bolton, Congressman from Ohio, (also introduced into the Senate as Joint Resolution 56, by Senator H. Alexander Smith) proposes the establishment of a National Commission on Nursing Services.

The function of the Commission would be to study on behalf of the public the entire field of nursing, determine the causes for the present nursing situation, and recommend in a report to the Congress what should be done about it.

Mrs. Bolton believes this Commission would point the way to further legislation—where it is

needed—for improving the health of the nation and to public understanding of areas in which the states and localities must take their own action.

Two similar national Commissions are now in operation; the Hoover Commission, studying the organization of the Executive Branch of the Government, and the Commission of Intergovernmental Relations, which is making a study of that field.

Among the members of the National Committee for a Commission on Nursing Services are: Chairman, Mr. Samuel Horwitz, Trustee, Mount Sinai Hospital, Cleveland, Ohio; Dr. David B. Allman, Chairman, Committee on Legislation, American Medical Association, Atlantic City, New Jersey; Miss Gertrude E. Cromwell, Supervisor of Nursing, Denver Public Schools, Denver, Colorado; Mrs. Howard Egert, President, Cleveland Federation of Women's Clubs, Cleveland, Ohio; Mr. Stanley Ferguson, Director, University Hospitals, Cleveland, Ohio; Dr. Charles Higley, Past President, Cleveland Hospital Service Association, Cleveland, Ohio; Mr. John R. Mannix, Director, Cleveland Hospital Service Association, Cleveland, Ohio; Mrs. R. Louise McManus Director, Division of Nursing Education, Teachers' College, Columbia University, New York, N. Y.; Dr. George Sackett, President, Cleveland Academy of Medicine, Cleveland, Ohio; Miss Hilda M. Torrop, Executive Director, National Association for Practical Nurse Education, New York, N. Y.; Mr. Samuel Whitman, Director, Cleveland Mental Health Association, Cleveland, Ohio; Mrs. Robert W. Woodruff, Atlanta, Georgia. The membership of this Committee is being expanded.

"America owes a great debt of gratitude to our nurses—a debt not only of gratitude, but of obligation," states Congressman Bolton. "Theirs is a service on behalf of the humanities. Their lives are dedicated to helping people who are sick and who are in trouble. For this we owe them eternal gratitude.

"But the obligation which our country owes the nurses has not yet been fulfilled. This obligation entails a fuller recognition of their services, a deeper understanding of the problems with which they are confronted, and the development of practical measures which will help them give to society the full measure of their specialized skills and experiences, as they themselves wish to do."

BONAMINE MEETS REQUIREMENTS OF 'IDEAL MOTION SICKNESS DRUG'

Bonamine closely meets the requirements set for an ideal prophylactic for motion sickness, according to Drs. J. W. Strode and M. W. Amster of Pfizer Laboratories, who have conducted a study of nine of the more commonly prescribed motion sickness remedies.

The physicians, reporting in a recent issue of the *International Record of Medicine and General Practice Clinics,** found that Bonamine approaches the standards generally set for a motion sickness drug in that it is inexpensive, effective in small dosages over a long period of time, and relatively free of side effects.

Drugs studied by Drs. Strode and Amster included diphenhydramine (Benadryl), dimenhydrinate (Dramamine), promethazine (Phenergan), cyclizine (Marezine), phenothiazine (Parsidol), pyrathiazine (Pyrrolazote), hyoscine, prophenpyridamine (Trimeton) and Bonamine (Pfizer Laboratories brand of meclizine hydrochloride).

The investigators point out that a major consideration in motion sickness research has been to find effective agents which are devoid of side effects, such as sedation—the only notable side effect of any of the motion sickness drugs.

Only Bonamine, cyclizine, and pyrathiazine were found relatively free of sedative effects. Of these three drugs, the physicians emphasized, Bonamine is the only one which has been thoroughly investigated and reported upon.

Published reports on the use of Bonamine in some 700 cases have shown that side effects in Bonamine-treated cases were no higher than in placebo-treated patients.

Generally, for protection over periods longer than six to eight hours, motion sickness drugs must be taken in doses of 25 to 100 mg. three times a day, the study showed.

The only exceptions to this rule are Bonamine, promethazine, and hyoscine. Bonamine has a 24-hour duration of action, promethazine is effective for 12 hours, and hyoscine (in small doses) can be taken every eight hours.

Summing up the results of their study, Drs. Strode and Amster conclude:

"From the standpoint of side effects, we have noted that six of the nine (drugs) cause a significant incidence of sedation and that only Bonamine has been clearly established as free of this effect.

"From the standpoint of the desirability of affording maximal protection over a long period of time with a single small dose, it is again only Bonamine that fulfills the requirements."

*Vol. 168, No. 2.

STERLING DRUG HONORS 2 EXECUTIVES ON COMPLETING 25 YEARS' SERVICE

New York—Two top executives of Sterling Drug Inc. were honored by the company's executive management on the occasion of completing one-quarter century of service with Sterling, at a luncheon held here recently at the Biltmore Hotel.

The executives honored were Harvey M. Manss, vice-president and a director of Sterling in charge of The Bayer Company Division, and Martin Lasersohn, M.D., executive vice-president of Winthrop-Stearns Inc., a Sterling subsidiary. James Hill, Jr., chairman and president of Sterling, headed the group attending the luncheon. The guests comprised Sterling's Executive Committee, officers of the Bayer and Winthrop-Stearns organizations and executives of other Sterling companies.

Mr. Manss joined Sterling in 1930 as merchandising manager, later serving as director of its new products division. In 1932 he was appointed sales manager of The Bayer Company. He was elected vice-president of that company in 1934, and chief executive officer in 1937, the position he has since held.

In 1941, Mr. Manss was elected a director of Sterling and, in 1943, vice-president.

Born in Cincinnati, Mr. Manss received his early education in that city and attended the University of Cincinnati for two years. He graduated from the University of Michigan with an A. B. degree in

1909. He spent the next 20 years as an advertising executive before coming to Sterling.

Dr. Lasersohn, executive vice-president of Winthrop-Stearns, was born in St. Louis. He received his degree in medicine in 1922 from Washington University School of Medicine. For the next three years he interned at Barnes Hospital in St. Louis and at the Medical College of Virginia, Hospital Division.

In 1926 Dr. Lasersohn entered private practice in Richmond as a specialist in internal medicine. He also served on the faculty of the Medical College of Virginia, becoming an associate professor of medicine. He came to Winthrop in 1930 as associate medical director and was named medical director in 1937. He was appointed assistant to the president of the company in 1943 and, in 1945, was elected executive vice-president.

Dr. Lasersohn is the author of a number of papers on internal medicine published in medical journals. From 1950 to 1954 he was chairman of the Scientific and Research Awards Committee of the American Pharmaceutical Manufacturers' Association.

TERRAMYCIN REPORTED MOST EFFICIENT DRUG FOR TREATMENT OF PINWORMS

Terramycin is the most efficient single drug for the eradication of pinworms, according to Drs. Elmer H. Loughlin and William G. Mullin, of the New York Medical College and the Flower and Fifth Avenue Hospitals, here.

In the current issue of *Antibiotic Medicine**, the two physicians report on a test of the broad-spectrum antibiotic on 92 patients with pinworm.

A seven-day course of treatment with Terramycin cleared 88 of the patients of the parasite, according to the investigators. Although there were instances of re-infection or relapse in some of the "cured" cases, the physicians said that Terramycin therapy is preferred for the eradication of pinworm.

Terramycin appears to arrest the development of the pinworm (Enterobius vermicularis) and thus prevents re-infection of the patient, Drs. Loughlin and Mullin state.

Scratching of the irritated perianal area by the patient contributes to re-infection. Pinworm eggs are caught under the fingernails and thus are transmitted back to the host and to others who come in contact with him.

The clinicians note a difference in action between Terramycin and the piperazine compounds that are used in the treatment of enterobiasis.

On the basis of these apparently different actions they suggest a combination of Terramycin and a piperazine compound might be highly effective, and that each also could be given for shorter periods of time.

Studies are now being conducted to determine the possibility of the synergistic action of these agents.
*Vol. 3, p. 145.

PFIZER OFFERS NON-CALORIC SWEETENER

New York, N. Y., May 1—Chas. Pfizer & Co., Inc., today announced the availability of the non-caloric sweetener, calcium cyclamate, for use in the preparation of dietetic products requiring low sugar content.

Long a manufacturer of citric and tartaric acids and other food and beverage ingredients, Pfizer stated that it will begin the marketing of calcium cyclamate at once through its Chemical Sales division.

Calcium cyclamate is completely stable, unaffected by heat or cold. It maintains its sweetening effect in canning, freezing and baking. Widely used in dietetic products—soft drinks, frozen desserts, jams, jellies and canned fruits—this non-nutritive sweetener is compatible with natural and artificial flavorings, leaves no bitter after-taste and is unaffected by fruit acids.

"The decision to add calcium cyclamate to our line is a logical one," Paul E. Weber, assistant divisional sales manager, stated. "We have been supplying food and beverage processors for nearly 100 years and the introduction of this product is in keeping with our policy of providing every possible service to the industry."

Pfizer will offer calcium cyclamate as a white free flowing material in 5, 25 and 100 pound fiber drums with polyethylene liners. Prices range from $3.85 per pound in five-pound containers to $2.95 per pound in 5,000 pound quantities.

NEW STERAJECT CARTRIDGE HAS STERILE NEEDLE ATTACHED

A new, improved Steraject disposable cartridge with sterile needle attached has been introduced here by Pfizer Laboratories, division of Chas. Pfizer & Co., Inc.

The new cartridge fits the regular Steraject syringe and is available with eight different antibiotic dosage forms.

Complete sterility is maintained until needle cover is removed, thereby decreasing danger of contamination of injection site.

Dosage forms available in the new cartridge include:

Procaine penicillin aqueous suspension in 300,000 units, 600,000 units and 1,000,000 units strengths, Permapen aqueous suspension, Permapen Fortified, Combiotic aqueous suspension, streptomycin sulfate solution (1 gm.) and dihydrostreptomycin sulfate solution (1 gm.)

With the new cartridge assembly, clogging of the inside of the needle caused by premature puncture is eliminated. Patient acceptability is increased by the use of smaller (22 gauge by 1½ inch) needles on most dosage forms.

The new cartridges are packaged with needles attached in strips of cellophane, five units in a strip, two strips to a package. They replace older assemblies at no increase in cost.

NEW GERIATRIC SUPPLEMENT, NEOBON, COMBATS PROBLEMS OF AGING

Chicago—Neobon Capsules, supplying five major factors to combat the most common problems of aging, have been introduced by J. B. Roerig, division of Chas. Pfizer, here.

The new product is designed to retard the aging process in the adult male and female, according to Dr. Thomas A. Garrett, medical director of Roerig.

It supplies, in a soft gelatin capsule, hormones, hematinics, digestant enzymes, proteins and nutritional supplements—each capable of relieving or preventing one or more of the undesirable features of the aging process.

Neobon can be used as an adjuvant to specific therapy. Because it combines in a single medication the five specific ingredients most frequently prescribed by physicians, Neobon saves the patient both time and money.

It has been accepted by the medical profession that decreased gonadol function occurs in the older adult and may be combatted successfully by daily administration of small amounts of estrogenic and androgenic substances. Three capsules of Neobon, the normal daily dose, contain recommended amounts of methyl testosterone and ethinyl estradiol.

In addition, Neobon contains hematinic factors such as iron, folic acid, vitamin B-12, vitamin C, a specially prepared liver-stomach substance, molybdenum, cobalt and copper. It prevents the development of ordinary iron deficiency and nutritional anemias which occur in a significant number of older adults.

Older adults frequently also suffer from the effect of general decrease in gastric and digestive enzyme function. To offset this, Neobon provides pepsin and pancreatic enzyme activity by the inclusion of pancreatic substance, liver-stomach substance and glutamic acid.

Dietary habits of the older adults often cause a high-quality protein deficiency due to excessive intake of "soft foods" such as breads, puddings and other products chiefly made from white flour.

Lysine in Neobon improves the quality of white flour protein consumed by the patient. Daily dosage of Neobon can raise the quality of this protein to the level of what normally would be obtained in several ounces of fresh meat.

To meet the special nutritional needs of the older patients, Neobon includes large amounts of the stress vitamins, ascorbic acid, niacinamide and pyridoxine.

Neobon is supplied in bottles of 60 soft, soluble capsules, on prescription only. Recommended daily dosage is one capsule, three times daily.

BONAMINE MOTION SICKNESS REMEDY NOW AVAILABLE IN CHEWING-GUM TABLET

A mint-flavored chewing-gum tablet containing the long-acting motion sickness drug Bonamine has been introduced by Pfizer Laboratories, division of Chas. Pfizer & Co., Inc., under the name Bonamine Chewing Tablets.

Incorporating 25 mg. of Bonamine in the sugar coating of the chicle base tablets, the new product is indicated for the prevention and treatment of motion sickness.

Bonamine Chewing Tablets offer the advantage of being particularly suitable for use while traveling, especially for children. The chewing-gum tablet form eliminates the need for water and thus frees the traveler from dependence on easy access to liquids.

Tests have shown that Bonamine is rapidly released from the tablet for almost immediate ingestion and absorption.

Clinical trials have shown that 25 mg. of Bonamine will protect the patient from motion sickness up to 24 hours. Side effects are minimal.

To prevent motion sickness, adults should chew one or two tablets one hour before departure. Dose can be repeated every 24 hours.

AMER. JOUR. DIG. DIS.

We thank you, doctor, for prescribing Trevidal. Most of you who have employed this new, balanced protective antacid have continued to use it routinely. For those of you who have not yet had a chance to evaluate the unique antacid activity of Trevidal, may we suggest you write us today for a clinical trial supply.

TREVIDAL®

	EACH TABLET CONTAINS:	
Unique vegetable mucin supplies protective coat to irritated stomach lining	Regonol*‡	100 mg.
Balance of ingredients avoids constipation, diarrhea, or alkalosis	Magnesium trisilicate	150 mg.
	Aluminum hydroxide gel	90 mg.
	Calcium carbonate	105 mg.
	Magnesium carbonate	60 mg.
Binder controls and extends antacid activity	Egraine†‡	45 mg.

AVAILABLE IN BOXES OF 100 TABLETS, SPECIALLY STRIPPED FOR EASY CARRYING

*Cyamopsis tetragonoloba gum †Protein binder from oat ‡Trade Marks

Organon INC. • ORANGE, N. J.

Available on prescription only, Bonamine Chewing Tablets are packaged in pliofilm strips of four tablets, two strips to a carton.

MANTOMIDE AND ERYTHROMYCIN MOST EFFECTIVE IN AMEBIASIS

New Orleans—Treatment of intestinal amebiasis with Erythromycin and Mantomide, an experimental amebicidal compound developed at the Sterling-Winthrop Research Institute, proved more effective in eradicating symptoms of the disease than other combinations of drugs tested, according to a group headed by Dr. Gordon McHardy of the Browne-McHardy Clinic.

Mantomide and Erythromycin had a combined therapeutic efficiency of 96.2 per cent, he states in *Antibiotic Annual* (p. 863, 1955). This figure was higher than for other combinations of antibiotic and chemotherapeutic agents studied, and higher than the effectiveness of the individual drugs.

In one series of ten patients, *Endamoeba Histolytica* was eradicated in every instance and no symptoms were observed at the end of a 20-day follow-up period. None of the group exhibited side effects. The series was subsequently expanded to include 26 patients, with an average follow-up period of 45 days. A recurrence rate of only 3.8 per cent was noted.

The ideal combination of drugs to treat the disease, the authors say, is a chemical agent, or directly-acting antibiotic without other antibacterial influence, combined with an innocuous, indirectly-acting antibiotic. Mantomide was selected for the combined study because it was 88 per cent effective against intestinal amebiasis when given alone. In these tests it had shown no side effects or indications of toxicity.

Unlike most amebicidal drugs, Mantomide contains no iodine or arsenic. Its action is specific, previous studies demonstrated, killing the parasites but leaving bacteria found in the intestine relatively unaffected.

Mantomide, synthesized at the Sterling-Winthrop Research Institute, is N-(2,4-dichlorobenzyl) -N-(2-hydroxyethyl) dichloroacetamide.

NEW PRESCRIPTION SPECIALTY: NEOBON CAPSULES

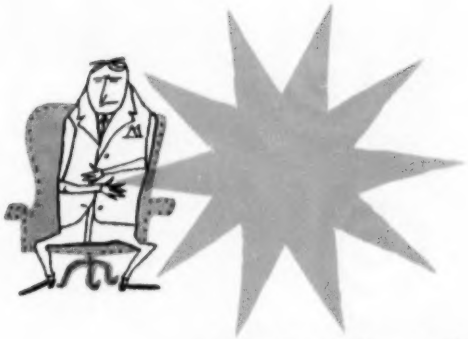
WHAT THE PRODUCT IS: Dark red, soft gelatin capsules containing lysine, methyl testosterone, ethinyl estradiol, liver-stomach substance, pancreatic substance, glutamic acid, rutin, ascorbic acid, folic acid, vitamin B-12, vitamins A, D, E, calcium pantothenate, vitamins B-1, B-2, B-6, niacinamide, iron, and eight trace elements.

WHAT IT'S FOR: As an agent to retard the aging process. Supplies five important factors needed to combat major problems of aging. (Hematinic component, hormonal replacement, digestant enzymes, nutritional supplement and protein supplement).

HOW ADMINISTERED: Orally, one capsule, three times daily, with meals.

HOW SUPPLIED: In bottles of 60 soft, soluble capsules. On prescription only.

WHO MAKES IT: J. B. Roerig & Co., Chicago 11, Illinois.



a new topical anesthetic for oral administration

XYLOCAINE® VISCOUS ASTRA

(Brand of lidocaine*)

the most effective anesthetic

for the proximal parts of the digestive tract

- Quick acting with prolonged effect
- High viscosity and low surface tension permit the anesthetic, Xylocaine Hydrochloride, to come into immediate and intimate contact with the mucous membranes
- Safe . . . nonirritating . . . nonsensitizing.
- Cherry flavored . . . pleasant and easy to take.
- Xylocaine Viscous has proved valuable in the "dumping" syndrome, hiccup, pyloric spasm caused by peptic ulcer, stomatitis, pharyngitis, esophagitis, acute cardiospasm, pylorospasm in infants, severe vomiting of pregnancy, esophagoscopy, gastroscopy, gastric intubation and gastric lavage.
- Contains 2% Xylocaine Hydrochloride in an aqueous solution adjusted to a suitable consistency with carboxymethylcellulose. Cherry flavored for palatability.

Supplied: In bottles of 100 and 450 cc.
Average Dosage: One tablespoonful, administered orally.
Additional information available upon request

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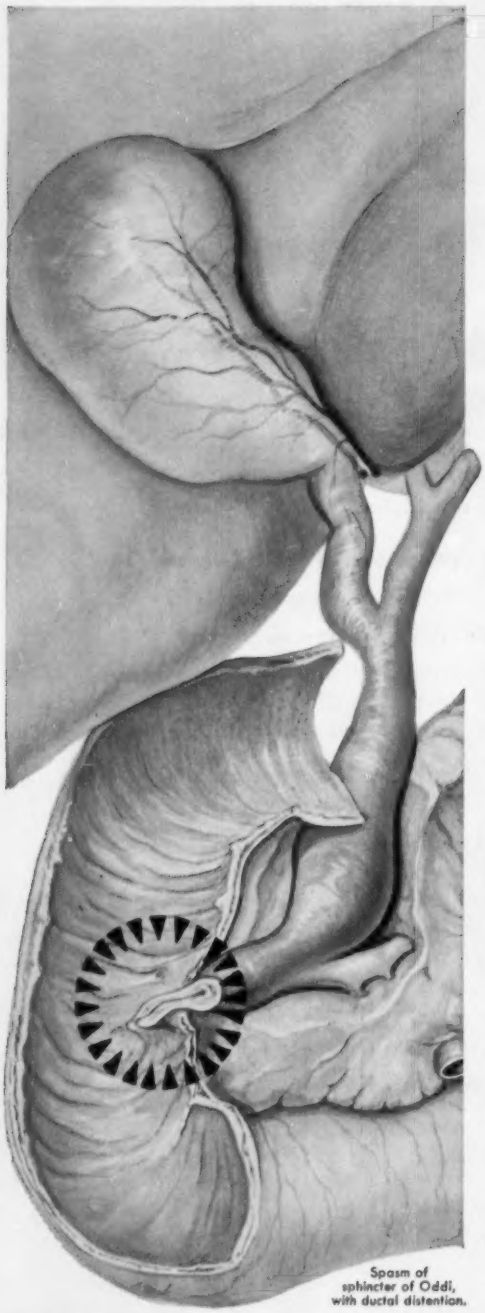
*U.S. Patent No. 2,441,498



Spasm of sphincter of Oddi, with ductal distention.

KETOCHOL® IN BILIARY STASIS

Rational Therapy in Biliary Dysfunctions

Ketochol contains all four unconjugated bile acids—not salts.

An inadequate flow of bile[1] into the intestine, caused by such conditions as severe liver disease, biliary fistulas, biliary obstruction and congenital atresia of the bile ducts, will eventually produce severe nutritional and digestive disturbances, anemia and a tendency toward abnormal bleeding.

Ketochol stimulates the flow of thin bile to "flush" the biliary passages. Ketochol relieves nausea, vomiting, pain and other symptoms of chronic inflammation of the gallbladder by its hydrocholeretic action.

Ketochol is well tolerated. The average dose is one tablet three times a day with meals, together with a suitable diet.

Ketochol is available in tablet form, 250 mg. (3¾ grains) of ketocholanic acids per tablet.

Adjunctive Antispasmodic-Sedative Therapy

Pavatrine® with Phenobarbital for selective control of smooth muscle spasm and for mild sedation of the nervous, tense patient is an excellent adjuvant in the management of biliary disorders. The average dose is one or two tablets three or four times daily, as needed.

Pavatrine with Phenobarbital contains 125 mg. (2 grains) of Pavatrine and 15 mg. (¼ grain) of phenobarbital per tablet. G. D. Searle & Co., Research in the Service of Medicine.

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1. Irvin, J. L.: The Secretion and Enterohepatic Circulation of Bile Acids: Replacement of Bile Acids in Biliary Insufficiency, North Carolina M. J. *13*:206 (April) 1952.

SEARLE